Congenital Anomaly Register & Information Service for Wales

caris review 2010

including data 1998 – 2009

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inside

GIG CYMRU NHS WALES

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Public Health Wales

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Foreword

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.

Welcome to the 2009 CARIS annual review.

This report includes a summary of congenital anomalies in Wales for the period 1998-2009. More detailed information and data tables are available from the CARIS website www.wales.nhs.uk/caris[1]. This year we include a special focus on facial and eye anomalies. These will also be featured in our 2010 annual meetings.

Once again we would like to thank all contributing health professionals for your ongoing support.

We are very grateful to the following people for their contributions to this report.

- Tracy Price, Hugo Cosh and members of the Public Health Wales Observatory Analytical Team for data analyses
- Siobhan Jones and Delyth Jones for work on cleft palate in North Wales
- Vanessa Hammond for the article on psychological issues
- Bethan Thomson for illustrations

Margery Morgan, Lead Clinician

Judith Greenacre, Director of Information

David Tucker, CARIS manager

The CARIS team.

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

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1 Also accessible through the HOWIS (NHS Wales) website www.howis.wales.nhs.uk/caris

Summary

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**

The following key points are based on twelve years of data now available (1998 – 2009). This includes a total of 19,634 cases (16,790 live born) out of 394,556 total births (live and stillbirths):

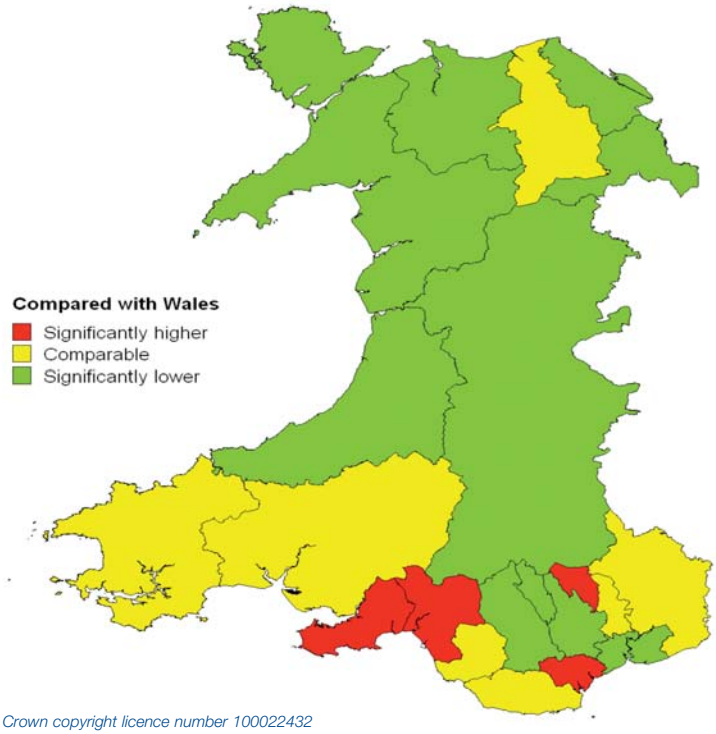
Patterns and clusters of anomalies

- **The gross[2] rate of congenital anomalies reported is 5.0%.**
- **The rate of congenital anomalies in live born babies is 4.3%.**
- **86% of cases are live born and 96% of these survive to the end of their first year. Survival is reduced with increasing complexity of anomalies.**
- **Congenital anomaly rates in Wales are often apparently higher than other areas of Europe or Britain.**
- **Variations in rates are again seen around Wales. In part this is due to differences in reporting and remains under review (Figure 1).**
- **Some specific anomalies continue to be investigated because of particularly high rates in Wales. These include gastroschisis and isolated cleft palate.**
- **Factors that 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 single group reported, followed by anomalies of the urinary tract, limbs and musculoskeletal system.**
- **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.**

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.**

Figure 1: Gross case rate per 10,000 total births, ranked Wales local authorities, 1998-2009



2 The gross rate includes all cases of anomaly recorded as miscarriages, terminations of pregnancy, live and stillborn babies.

CARIS activity 2009

Wales

CARIS became part of Public Health Wales NHS Trust on October 1st 2009.

Annual meetings were held in the Riverfront Centre, Newport and the University Of Wales, Bangor. The focus of these was skeletal anomalies.

United Kingdom

CARIS continued to contribute to the British Isles Network of Congenital Anomaly Registers (BINOCAR). David Tucker chairs the coding working group and sits on the management committee.

Congenital Anomalies and Socioeconomic Deprivation in Wales 1998-2007
CARIS presented a poster at the UK Public Health Association Conference in Brighton (April 2009).

International

Congenital anomalies, smoking, and deprivation in Wales 1998–2008
This poster was presented at the European Collaboration of Congenital Anomaly Registers (EUROCAT) conference in Bilbao, June 2009.

Outcome of antenatally suspected congenital cystic adenomatoid malformation of the lungs (CCAM) and sequestration of the lungs in Wales, UK: 7 years experience
Gopal Krishnan presented this paper at the International Clearing House of Birth Defects, Surveillance and Research (ICBDSR) meeting in Salt Lake City, September 2009

Outcome of antenatally suspected sequestration of lung
This was presented as a poster at the 9th World Congress of Perinatal Medicine, Berlin, October 2009.

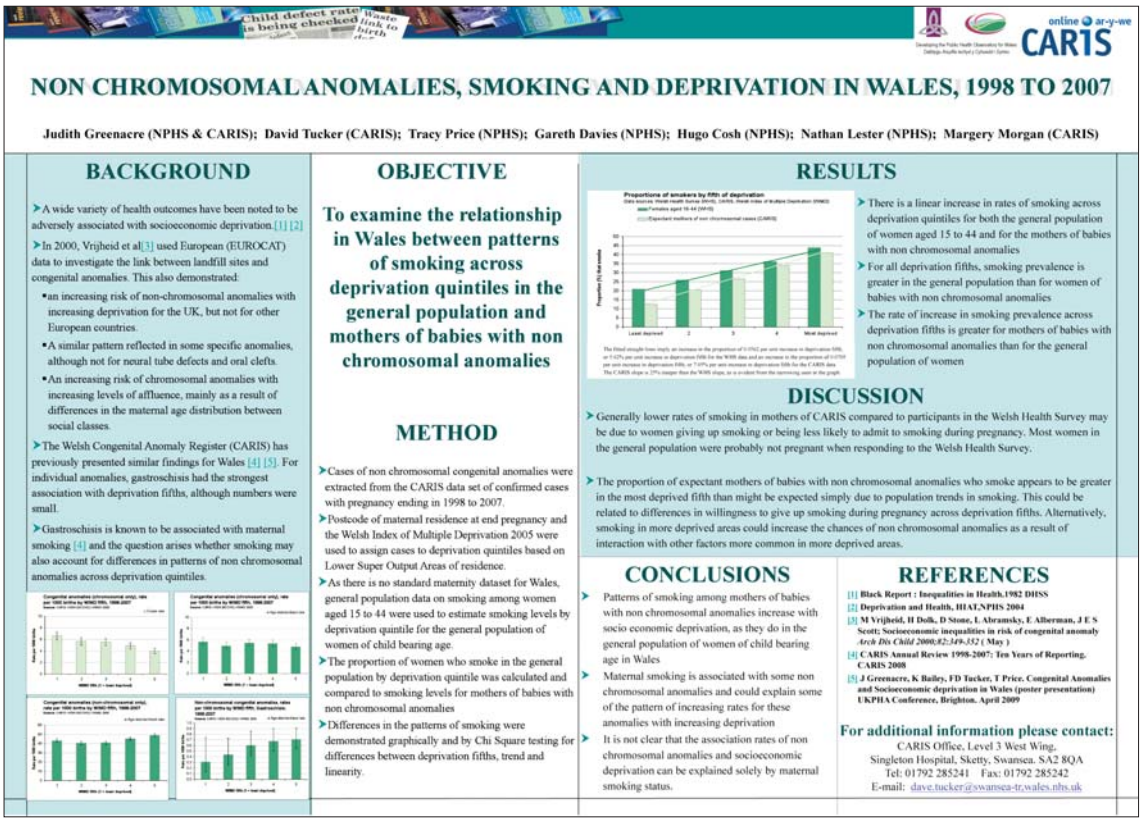
David Tucker joined the coding group of ICBDSR.

Websites

www.binocar.org.uk

www.eurocat-network.eu

www.icbdsr.org



NON CHROMOSOMAL ANOMALIES, SMOKING AND DEPRIVATION IN WALES, 1998 TO 2007

Judith Greenacre (NPHS & CARIS); David Tucker (CARIS); Tracy Price (NPHS); Gareth Davies (NPHS); Hugo Cosh (NPHS); Nathan Lester (NPHS); Margery Morgan (CARIS)

BACKGROUND

- A wide variety of health outcomes have been noted to be adversely associated with socioeconomic deprivation.[1] [2]
- In 2000, Vrijheid et al[3] used European (EUROCAT) data to investigate the link between landfill sites and congenital anomalies. This also demonstrated:
  - an increasing risk of non-chromosomal anomalies with increasing deprivation for the UK, but not for other European countries.
  - A similar pattern reflected in some specific anomalies, although not for neural tube defects and oral clefts.
  - An increasing risk of chromosomal anomalies with increasing levels of affluence, mainly as a result of differences in the maternal age distribution between social classes.
- The Welsh Congenital Anomaly Register (CARIS) has previously presented similar findings for Wales [4] [5]. For individual anomalies, gastroschisis had the strongest association with deprivation fifths, although numbers were small.
- Gastroschisis is known to be associated with maternal smoking [4] and the question arises whether smoking may also account for differences in patterns of non chromosomal anomalies across deprivation quintiles.

OBJECTIVE

To examine the relationship in Wales between patterns of smoking across deprivation quintiles in the general population and mothers of babies with non chromosomal anomalies

METHOD

- Cases of non chromosomal congenital anomalies were extracted from the CARIS data set of confirmed cases with pregnancy ending in 1998 to 2007.
- Postcode of maternal residence at end pregnancy and the Welsh Index of Multiple Deprivation 2005 were used to assign cases to deprivation quintiles based on Lower Super Output Areas of residence.
- As there is no standard maternity dataset for Wales, general population data on smoking among women aged 15 to 44 were used to estimate smoking levels by deprivation quintile for the general population of women of child bearing age.
- The proportion of women who smoke in the general population by deprivation quintile was calculated and compared to smoking levels for mothers of babies with non chromosomal anomalies
- Differences in the patterns of smoking were demonstrated graphically and by Chi Square testing for differences between deprivation fifths, trend and linearity.

RESULTS

- There is a linear increase in rates of smoking across deprivation quintiles for both the general population of women aged 15 to 44 and for the mothers of babies with non chromosomal anomalies
- For all deprivation fifths, smoking prevalence is greater in the general population than for women of babies with non chromosomal anomalies
- The rate of increase in smoking prevalence across deprivation fifths is greater for mothers of babies with non chromosomal anomalies than for the general population of women

DISCUSSION

- Generally lower rates of smoking in mothers of CARIS compared to participants in the Welsh Health Survey may be due to women giving up smoking or being less likely to admit to smoking during pregnancy. Most women in the general population were probably not pregnant when responding to the Welsh Health Survey.
- The proportion of expectant mothers of babies with non chromosomal anomalies who smoke appears to be greater in the most deprived fifth than might be expected simply due to population trends in smoking. This could be related to differences in willingness to give up smoking during pregnancy across deprivation fifths. Alternatively, smoking in more deprived areas could increase the chances of non chromosomal anomalies as a result of interaction with other factors more common in more deprived areas.

CONCLUSIONS

- Patterns of smoking among mothers of babies with non chromosomal anomalies increase with socio economic deprivation, as they do in the general population of women of child bearing age in Wales
- Maternal smoking is associated with some non chromosomal anomalies and could explain some of the pattern of increasing rates for these anomalies with increasing deprivation
- It is not clear that the association rates of non chromosomal anomalies and socioeconomic deprivation can be explained solely by maternal smoking status.

REFERENCES

[1] Black Report : Inequalities in Health.1982 DHSS
[2] Deprivation and Health, HIAT,NPHS 2004
[3] M Vrijheid, H Dolk, D Stone, L Abramsky, E Alberman, J E S Scott; Socioeconomic inequalities in risk of congenital anomaly *Arch Dis Child 2000;82:349-352* (May)
[4] CARIS Annual Review 1998-2007: Ten Years of Reporting. CARIS 2008
[5] J Greenacre, K Bailey, FD Tucker, T Price. Congenital Anomalies and Socioeconomic deprivation in Wales (poster presentation) UKPHA Conference, Brighton. April 2009

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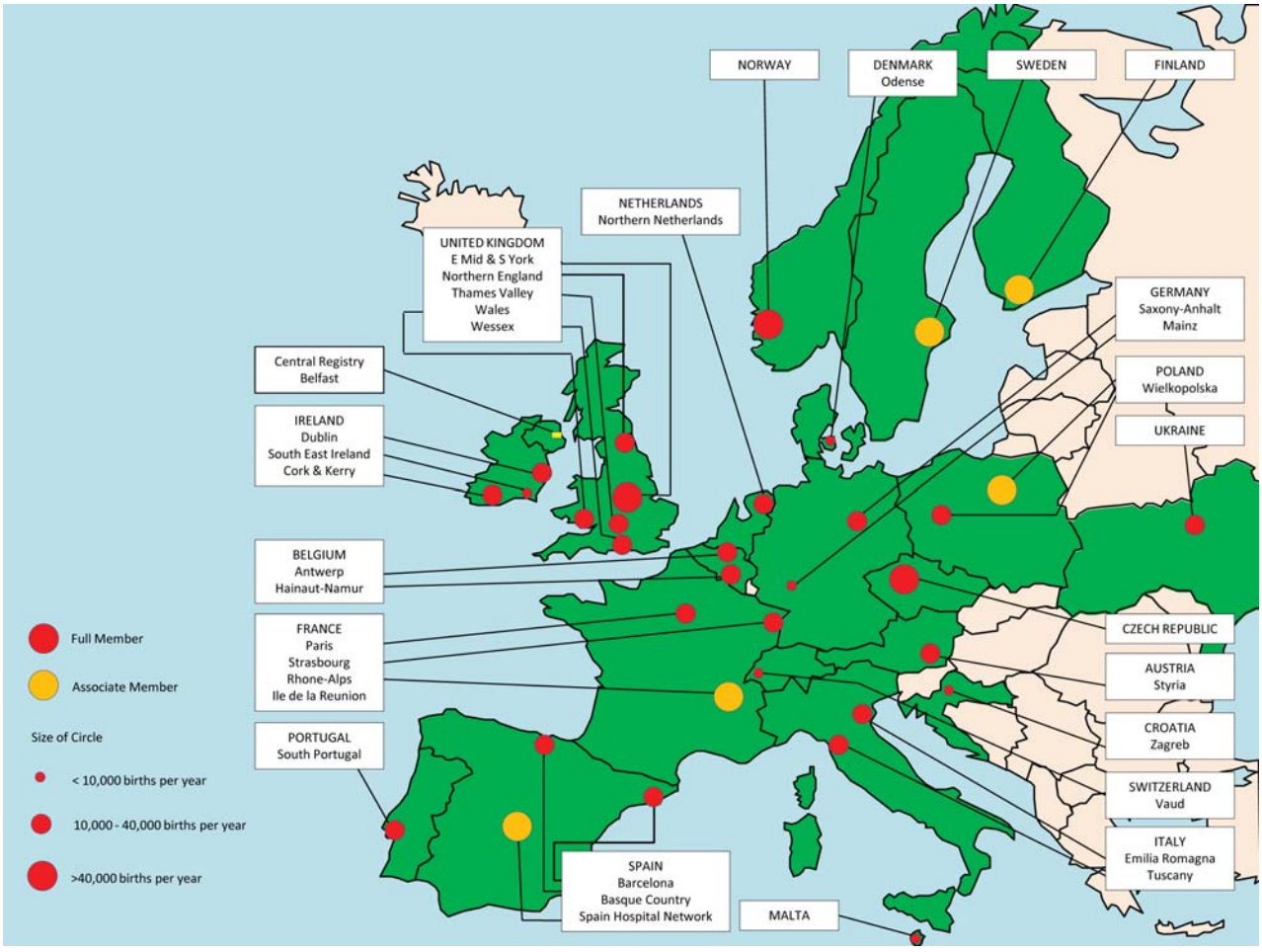
CARIS activity 2009

Publications in 2009 using CARIS data

- *Congenital Abnormalities: Data Needed to Establish Causes, BMJ, Vol 339, pp 3428* Draper ES, Rankin J, Tonks A, Boyd P, Wellesley D, Tucker D, Budd J, BINOCAR Management Committee (2009)
- *Congenital Hydronephrosis: Prenatal Diagnosis and Epidemiology in Europe, Journal of Pediatric Urology, Vol 5, pp 47- 52.* Garne E, Loane M, Wellesley D, Barisic I and a EUROCAT Working Group (2009)
- *Maternal Age-Specific Risk of Non-Chromosomal Anomalies, British Journal of Gynaecology, Vol 116, pp 1111-1119* Loane M, Dolk H, Morris JK and a EUROCAT Working Group (2009)
- *Special Report: The Status of Health in the European Union: Congenital Malformations, EUROCAT Central Registry, University of Ulster*. EUROCAT (2009)
- *Special Report: Congenital Heart Defects in Europe, 2000-2005, EUROCAT Central Registry, University of Ulster*. EUROCAT (2009)

Map of EUROCAT Registries



Development of the face and eyes

Facial development

Structures of the face, neck, cranial nerves and arteries of the upper chest all form from the embryological system of branchial arches and pouches present by the third to fourth week of gestation (see figures 2 and 3). The face is formed between the fourth and tenth week of pregnancy. The first arch is particularly relevant for facial structure and gives rise to the maxillary and mandibular architecture.

Figure 2: Embryonic head at five weeks

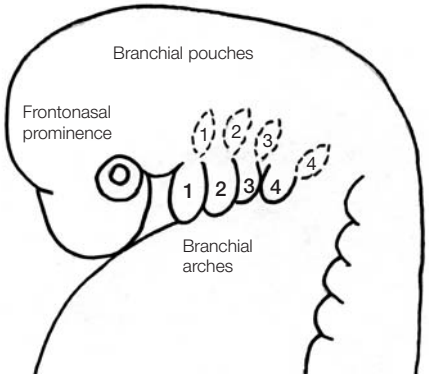


Table 1: Milestones in facial development

3rd week gestation	Inner ear developing from the otic placode. Middle ear developing from maxillary swelling.
4th week	Eyes appear as lateral grooves which form the optic vesicle.
5th week	Frontonasal process develops 2 swellings, the nasal processes.
6th and 7th week	Medial nasal processes fuse to form central part of nose. Lateral nasal processes form nostrils. Auricular swellings appear.
8th and 9th week	Medial walls of maxillary swellings form palatine shelves. Optic vesicle has developed optic cup and lens. Eyelids forming (fused until 20 weeks). Inner and middle ear developed.
10th week	Maxillary swellings have fused in midline forming philtrum of upper lip and primary palate. Palatine shelves have fused in midline forming secondary palate. Maxillary and mandibular swellings form upper and lower jaws. Nasal septum has grown to separate left and right nasal passages. Ear pinna fused from auricular swellings.

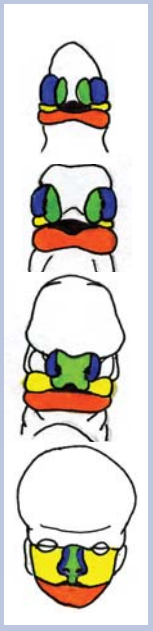
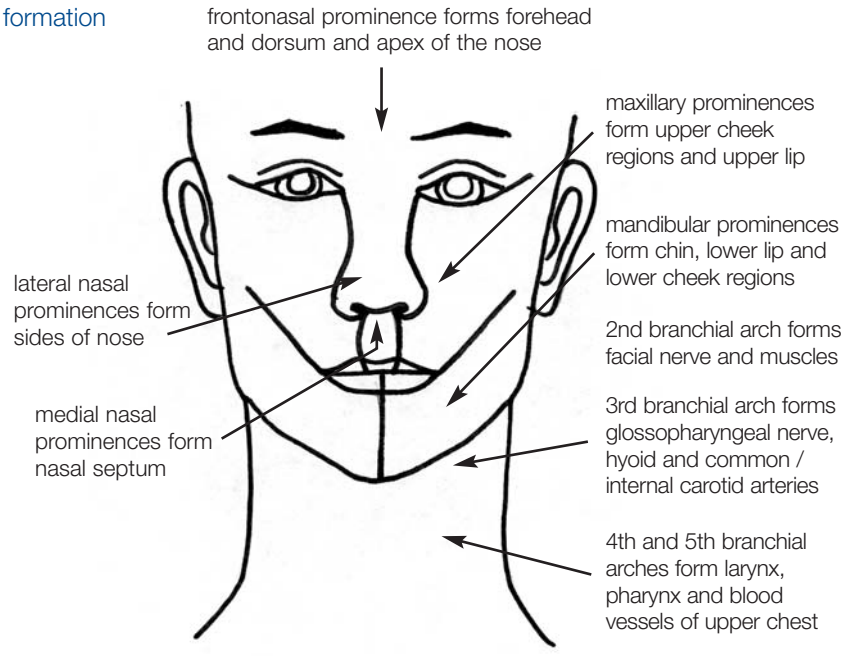


Figure 3: Summary of face formation



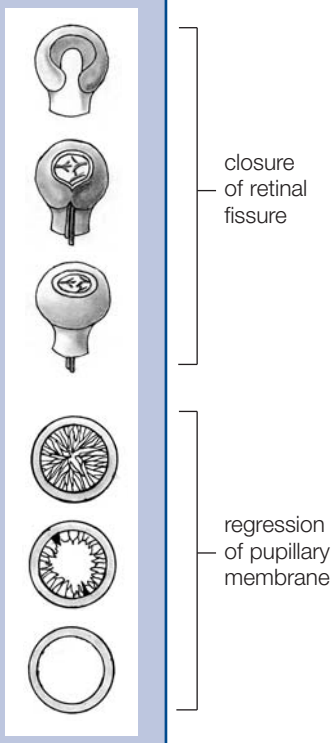
Development of the face and eyes

Eye Development

The eye is one of the first organs recognizable in the developing embryo. Its complex development relies on a series of events taking place correctly. Problems with development contribute to the congenital ocular anomalies seen in babies and children. Vision continues to develop after birth.

Table 2: Milestones in eye development

Fetal development	
Week 3	Optic groove forms in the forebrain.
Week 4	Optic cup develops. Lens and retina start development.
Week 5	Retinal fissure closes, incorporating optic nerve and blood supply; structures of face and orbit develop.
Week 6	First eyelid folds and nasolacrimal ducts develop.
Week 7	Eye now has an optic nerve, two layer retina and lens.
Week 8	Lacrimal gland develops.
Month 3	Eyelids fuse.
Month 4	Iris and vitreous develops; cornea and retina differentiate.
Month 5	Eyelids start to separate.
Month 6	Nasolacrimal duct patent; pupillary membrane still intact.
Month 7	Iris completes its pigmentation; pupillary membrane regresses.
Month 8	Iris sphincter working; lens diameter 5mm.
Month 9	Retinal blood supply in place.
After Birth	
10 weeks old – optic nerve myelination complete	



Identifying facial and eye anomalies

Some facial and eye anomalies may be seen on antenatal ultrasound. Neonatal examination of the newborn remains the main method of identification.

It is important to look at the face on antenatal ultrasound as facial anomalies have a strong association with complex syndromes and chromosomal disorders. Awareness of an isolated facial defect can help prepare parents before birth and allow time for appropriate counselling or discussion of treatment options.

Antenatal scanning of the face can be time consuming and difficult, depending on the fetal position (Table 3). The advent of 3D imaging can be helpful for parents and paediatric surgeons alike.

Facial mapping terms

- Hypertelorism – increased distance between the eyes
- Hypotelorism – decreased distance between the eyes
- Blepharophimosis – narrowed palpebral fissures
- Synophrys – medial fusion of the eyebrows
- Nasal bridge – upper part of nose between eyes
- Ala nasi – lateral border of the nostril
- Columella – medial part or septum of nostril
- Philtrum – vertical folds on upper lip

Table 3: Ultrasound of face and eyes

Orbits	Should be equal size
Interorbital distance	Should be roughly equal to orbital diameter to exclude hypertelorism / hypotelorism
Lenses	Should be anechoic; an echo suggests cataract
Lips	Look coronally and sagitally to exclude clefting
Mandible	Use profile view, should form a smooth curve from forehead to mandible; flat profile seen in chromosomal anomalies
Ears	Check for both ears and relationship to temporal bone to exclude low set ears

Newborn examination of face and eyes

Methods for examining the face and eyes are well described as part of the routine examination of the newborn. This is summarised in Figure 4.

Figure 4: Newborn examination of face and eyes

Overall
Inspect face for any unusual appearance, asymmetry or anomaly. Compare to parental facies if required.

Eyes
Check size and position, including distance of separation. Sclera should be white (blue in osteogenesis imperfecta).

Iris - normally blue and circular with pupil in centre. Look for Brushfield's spots (Down syndrome).

Lens - should be clear (clouded in glaucoma or cataract).

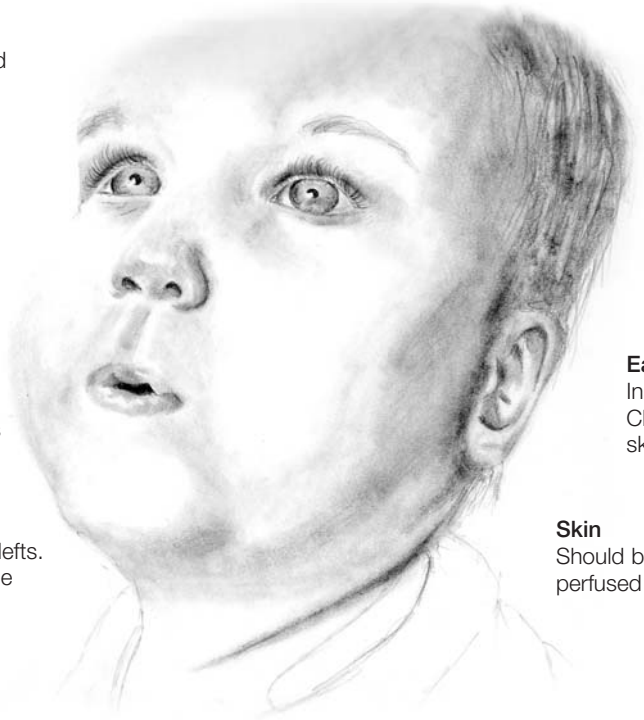
Check for red reflex (absent in cataract or retinoblastoma).

Mouth
Inspect gums for cysts, clefts and neonatal teeth.

Inspect tongue for size, cysts and dimples.

Examine palate to uvula for clefts. Palpate hard palate to exclude submucous defect.

Inspect lips for defects.



Structures around eyes
Check epicanthic folds; eyelids and eyebrows; slant of palpebral fissures (opening between eyelids).

Nose
Check patency of airway in each nostril.

Ear
Inspect size, shape, position. Check for abnormalities including skin creases, dimples and skin tags.

Skin
Should be uniform in colour, well perfused and free from swelling.

Causes of congenital anomalies of the eyes and face

As the development of the face and eyes is so complex there are many opportunities for anomalies to occur. Most of them are rare. The eye is very sensitive to the teratogenic effects of infectious agents and drugs (Table 4), the most serious defects occurring during the 4th to 6th week of development.

Maternal rubella infection (German measles) in the first trimester of pregnancy gives the fetus a 20% risk of being infected. Congenital rubella syndrome includes cataracts, cardiac defects and deafness. Other eye anomalies can include microphthalmos, glaucoma and pigmented retinopathy. The vaccination programme has markedly reduced the prevalence of the syndrome.

Toxoplasmosis can be caught by eating raw or poorly cooked meat or close contact with infected domestic animals, usually cats. The parasite crosses the placenta and infects the fetus causing microphthalmos and chorioretinitis.

There are many complex syndromes and genetic defects that also give rise to facial anomalies. For example, clefting and micrognathia are associated with syndromes such as triploidy, Edwards, and Treacher Collins (Figure 5).

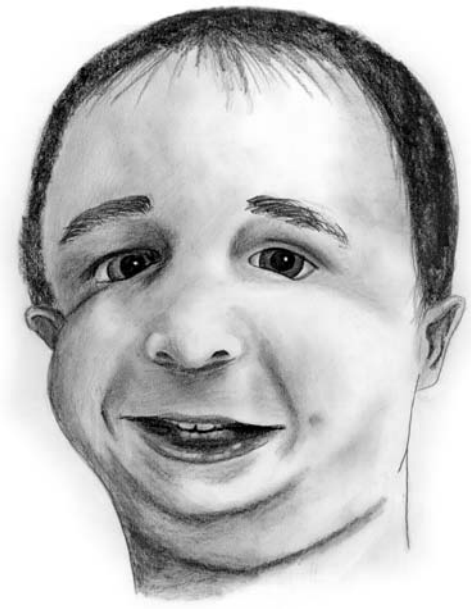


Figure 5: Treacher Collins syndrome

Table 4: Teratogens and infections that cause face and eye anomalies

Teratogens	
Alcohol	Ocular anomalies; short palpebral fissures; smooth philtrum
Isotretinoin	Craniofacial anomalies; cleft palate
Methotrexate	Craniofacial anomalies
Phenytoin	Fetal hydantoin syndrome with inner epicanthal folds, eyelid ptosis, broad depressed nasal bridge, phalangeal hypoplasia
Tetracycline	Stained teeth; hypoplasia of enamel
Thalidomide	Facial anomalies
Sodium valproate	Craniofacial anomalies
Warfarin	Nasal hypoplasia and eye anomalies
Infections	
Cytomegalovirus	Chorioretinitis
Herpes Simplex virus	Chorioretinitis
HIV	Prominent boxlike forehead; flattened nasal bridge; hypertelorism; triangular philtrum; patulous lips
Human Parvovirus B19	Eye defects
Rubella virus	Cataract; microphthalmos; glaucoma; pigmented retinopathy; tooth defects
Toxoplasma Gondii	Microphthalmos; chorioretinitis
Treponema Pallidum (syphilis)	Abnormal teeth
Varicella virus (chicken pox)	Cataracts; microphthalmos; Horner syndrome; optic atrophy; nystagmus; chorioretinitis

Eye Anomalies

Congenital Cataracts

These are opacities of the crystalline lens and can cause a legacy of blindness in one third of children. Bilateral cataracts are more common than unilateral.

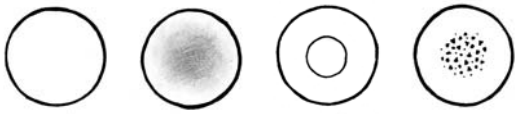
Cataracts account for about 30% of congenital eye malformations in liveborn babies. Around one fifth of cases have a family history of congenital cataract[3]. The world literature suggests a prevalence of around 3 per 10,000 births. CARIS data confirms this figure (Table 5).

Early detection and treatment are very important in determining the eventual visual outcome.

Antenatal Detection

Both lenses should be demonstrated when the fetal face is being visualized. They should appear anechoic, with no density echoes visible. Cataracts have been identified with various echoes including a double ring, diffuse opacification, or central densities (Figure 6).

Figure 6: Ultrasound appearances of fetal lens



Normal | Diffuse opacification | Double ring | Central densities

Causes of Congenital Cataracts

- Intrauterine infections
- Metabolic disorders
- Inherited genetic conditions
- Chromosomal syndromes
- Renal disease
- Skeletal disease
- Neurometabolic disease
- Muscular dystrophy
- Dermatological conditions

Management

Surgical treatment is recommended if there is significant impairment of vision. This involves removal of the lens resulting in a child needing to wear spectacles for reading and distance vision.

Early surgery can give excellent results in babies with bilateral cataracts and seriously reduced vision. A congenital cataract can cause a failure to develop the fixation reflex with the onset of nystagmus. Early surgery within the first 3 months of life is essential for the baby to develop fixation and binocular reflexes.

Congenital glaucoma

This is caused by a congenital anatomical anomaly in the angle of the anterior chamber which interferes with drainage of the aqueous humor. This defect is present at birth but enlargement of the eye does not appear until the child is at least a few months old.

Congenital glaucoma has an autosomal recessive pattern of inheritance. Prevalence is generally estimated around 1 per 10,000 births in western countries but with much higher rates in the Middle East and Slovakian gypsies[4]. Welsh rates are comparable at 0.8 per 10,000 total births.

Clinical features

The eye becomes large (buphthalmos) and the baby may be photophobic. All infants with apparently large eyes should be assessed for congenital glaucoma. An ophthalmic examination is needed if the width of the cornea is above 11mm as surgery will be necessary to save the baby's vision. If not diagnosed, the cornea becomes cloudy because of the swelling and can become totally opaque.

Management

Drainage and lowering of the pressure in the eye is necessary. Removing meshwork in the anterior chamber with a peripheral iridectomy can do this. Early treatment is necessary as complete blindness will ensue otherwise.

Retinoblastoma

This is the most common malignant intraocular tumour in childhood with an incidence of 1/15,000 to 20,000 live births in Europe[5]. CARIS data suggests rates in Wales of 0.6 per 10,000 total births or 1 in 16,700 births. The condition develops from the retinoblasts and can be present at birth. It is usually diagnosed before the third year of life. It is an unusual tumour having both hereditary (passed from parent to offspring) and familial (occurs more often in families) influences. The tumour is also unusual in that it is multifocal. 25% of cases are bilateral.

The tumour arises in the retina. It starts as small elevations on the retina which grow between the retina and the choroid (causing retinal detachment) or may grow inwards into the vitreous humor.

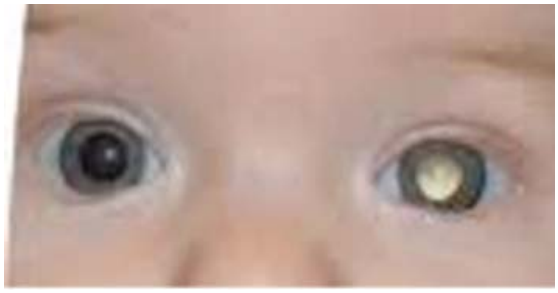
3 www.rnib.org.uk 4 J Med Genet 1999;36:290–294

5 http://www.orpha.net/

Eye Anomalies

Parents may notice whitening of the pupil (leukokoria) and loss of the red reflex (Figure 7), opacity, squint or poor vision in the affected eye.

Figure 7: Absent red reflex and leukokoria with retinoblastoma (left eye)



Management

If diagnosis is early then radiation alone may be sufficient. Surgery involving enucleation of the eye is necessary if diagnosed later. If left untreated the condition is fatal. Close follow up is essential and genetic counselling advisable for the family.

Microphthalmos and anophthalmos

These rare conditions can be associated with chromosomal disease, genetic syndromes and intracranial abnormalities.

In both conditions the orbit is small but the lens is present in microphthalmos, distinguishing it from anophthalmos (caused by failure of formation of the optic pit and outgrowths from the forebrain). If the orbit measures small against nomograms of orbital measurements then the fetus should be inspected for any other anomalies and possibly the karyotype checked.

Congenital Ptosis

This is the commonest developmental anomaly of the eyelids and usually occurs as an isolated finding (Figure 8). It can be associated with marked epicanthal folds and squint, digit anomalies, or as part of Turner's syndrome.

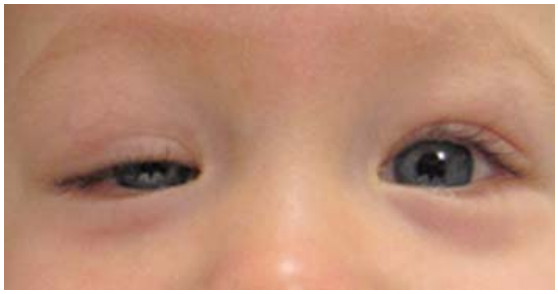
Congenital ptosis is usually unilateral and is thought to have a genetic component. Most children have normal binocular vision.

The Marcus Gunn jaw-winking syndrome involves elevation of the drooping eye lid on opening the mouth or lateral movement of the jaw.

Management

Surgery is best avoided unless there is interference with vision when the lid covers the pupil.

Figure 8: Congenital ptosis of right eye



Congenital coloboma

Congenital anomalies of the iris are common, particularly a sector coloboma of the lower part of the iris (Figure 9). This can be familial. Vision is usually unaffected but it can be associated with other ocular anomalies. At 1 per 10,000 births, Welsh rates appear similar to those in the published literature.

Figure 9: Coloboma

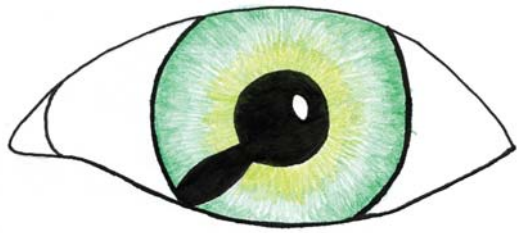


Table 5: Birth prevalence of selected eye conditions

Condition	Estimates from published literature Rate per 10,000 births	CARIS data 1998-2009 Gross rate per 10,000 total births
Congenital cataracts	1.2-6 (US data)[6]	3.6
Congenital ptosis	unknown	3.4
Congenital coloboma	1[7]	1.1
Congenital glaucoma	1[8]	0.8
Retinoblastoma	0.5 to 0.8[9]	0.6

6 http://emedicine.medscape.com/ 7 http://www.rnib.org.uk/ 8 *J Med Genet* 1999; 36: 290–294 9 http://www.orpha.net/

Facial Anomalies

These can be divided into four main groups:

- Otocraniofacial syndromes
- Facial clefting
- Mid-face syndromes
- Craniosynostosis syndromes

Otocraniofacial syndromes

Micrognathia

The mandible is formed from the first branchial arch (Figure 2). Damage to the blood supply is thought to result in underdevelopment of the first arch leading to craniofacial microsomia with a small receding jaw (Figure 10).

Marked micrognathia is seen in many chromosomal and genetic syndromes (Table 6). Respiratory difficulties can occur so a paediatric presence at delivery is essential in case endotracheal intubation is required.

Figure 10: Micrognathia in Pierre Robin sequence

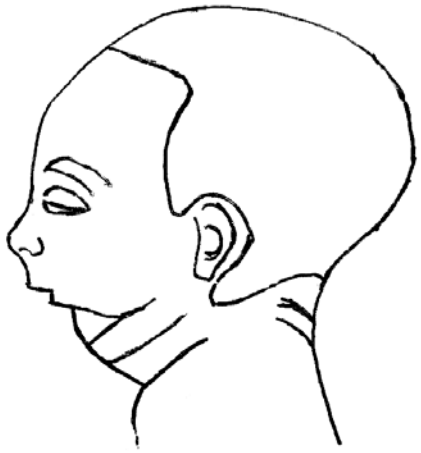


Table 6: Some syndromes associated with micrognathia

Syndrome	Genetic basis	Key features	Prevalence
Edwards syndrome	Trisomy 18	Micrognathia can occur in 50% cases	CARIS gross rate 6 per 10,000 total births but only 20% liveborn
Treacher Collins syndrome (Figure 5)	Autosomal dominant gene on long arm of chromosome 5	Underdeveloped lower jaw, ears, cheekbones & orbits, giving downward slant to eyes; large beak like nose; large mouth; cleft palate; occasional thumb deformity	Literature suggests 0.1 to 0.5/10,000 total births. 2 cases reported CARIS 1998 – 2009 (expected number from literature 4+)
Goldenhar syndrome or oculo-auriculo-vertebral spectrum (OAVS)	Sporadic	Underdevelopment of face, especially ears, jaw and cheek. Defects often unilateral and asymmetrical. Causes deafness, speech and swallowing problems. Can be associated with defects of neck vertebrae, heart and kidney	Literature suggests 0.1 to 0.9/10,000 total births. 16 cases reported CARIS 1998 – 2009 or 0.4/10,000 total births
Pierre Robin sequence – a range of entities associated with abnormal facial development (Figure 10)	Usually sporadic	Small jaw associated with glossoptosis (base of tongue falls back into throat) and cleft palate. Associated with varying degree of feeding and breathing difficulties. Syndromic and non syndromic forms exist	Published estimates overall of 0.3 to 5 per 10,000 total births. CARIS reports 66 cases or 1.7/10,000 total births. Differences in definition make comparisons difficult
Di George syndrome / velo-cardio-facial syndrome	One of a range of conditions associated with 22q11 deletion syndrome	Associated with low set ears, hypertelorism, cleft palate and cardiac anomalies	Approx 1-2.5/10,000 total births[10]. CARIS reports 52 cases with a rate of 1.3 per 10,000 births

10 Arch Dis Child. 2004 Feb; 89(2):148-51.

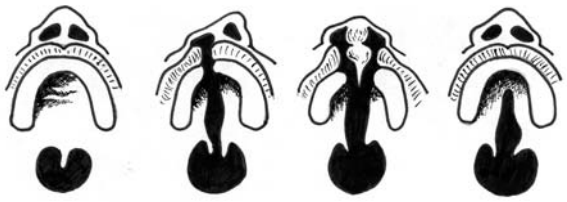
Facial Anomalies

Facial clefting

This is the most common anomaly of the face.[11] Cleft lip and cleft palate may occur in isolation or together and may be associated with other facial defects.

- Defects involving a cleft lip result from failure of the median nasal swellings to fuse with the maxillary swellings. They occur in about 1/1000 livebirths with higher levels in some racial groups and with boys affected more often than girls. About 13% of cases are associated with other anomalies. Unilateral cleft lip is more common than bilateral and the left side is more commonly affected than the right. Risk factors include maternal smoking, excess alcohol intake and anticonvulsant medication. Maternal folic acid reduces the risk.
- Isolated cleft palate arises from failure of formation of the palatal shelf (see Table 1). This arises in up to 1 in 2000 livebirths with no racial preference. Girls are more frequently affected than boys. About 50% are associated with other anomalies, especially chromosomal defects. Risk factors include increased maternal age, maternal smoking, alcohol and anticonvulsants. Folic acid does not reduce the risk.

Figure 11: Examples of cleft lip and palate



normal | unilateral cleft lip & palate | bilateral cleft lip & palate | isolated cleft palate

Table 7: Anomalies associated with facial clefting

- Trisomy 13; 18; 21
- Triploidy
- Holoprosencephaly
- Amniotic band syndrome – varied, complex defects
- Ectodermal dysplasia syndrome – autosomal dominant with limb defects
- Miller syndrome – autosomal recessive with acrofacial dysostosis
- Robert's syndrome - associated with micrognathia and limb defects
- Mohr syndrome – autosomal recessive – orofacial and digital defects
- Frontonasal dysplasia – associated hypertelorism

Ultrasound challenges

Most antenatal diagnosis takes place at the 20 week scan. A coronal scan will show a vertical transonic area within the upper lip, usually to the left of the midline. A transverse scan can show an alveolar defect if the palate is involved. A bilateral cleft lip and palate results in a mass in the centre of the upper lip which can be seen as an echodense area.[12]

3D scanning can be of great value in demonstrating facial clefting.

An isolated cleft palate can be very difficult to diagnose as usually the posterior part of the palate is involved. Colour flow Doppler may help if performed during fetal swallowing to assess the palate. Magnetic resonance may also be helpful.

The focus on scanning after finding a cleft involves a search for other anomalies, because of an increased incidence of associated defects (particularly chromosomal disorders and heart anomalies).

11 Bernheim N, Georges M, Malevez C, De Mey A, Mansbach A (2006) Embryology and epidemiology of cleft lip and palate. **B-ENT** Vol.2 Suppl. 4. Pg. 11-19

12 Textbook of Fetal Anomalies. Twinning P., McHugo J., Pilling D., 2007 Churchill Livingstone

Facial Anomalies

Problems with Clefts

- Feeding difficulties – mainly in cleft palate. May need special bottles
- Ear infections and hearing loss – mainly in cleft palate. Annual checks of middle ear required to check for fluid build up
- Speech difficulties – worse in cleft palate with nasal speech and consonant difficulties
- Dental problems – some clefts affect the gum resulting in missing teeth

Treatment of the infant with a cleft

The best treatment for a baby with a cleft involves a multidisciplinary approach with a paediatrician, plastic surgeon, dentist, ENT specialist, speech therapist, audiologist, genetic counsellor, psychologist and social worker.

Surgery can correct a cleft lip and palate. The lip is usually repaired at 3 months of age. If there is a cleft palate this is repaired between 6 and 18 months of age.

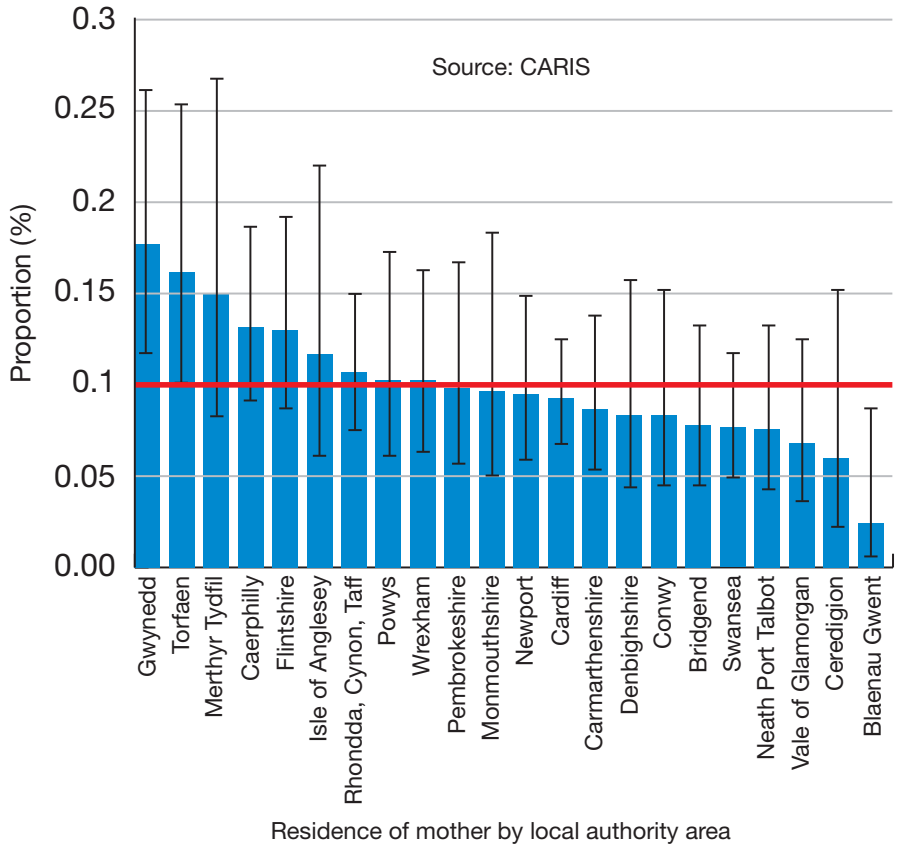
Cleft Palate in Wales: an update

CARIS data shows facial clefts occurring in 69 cases per year that come to the attention of health services (gross rate is 20.9 per 10,000 total births). Approximately 80% of cases are liveborn. Cleft lip with or without cleft palate is more common than cleft palate alone (Appendix A).

In 2003, CARIS undertook a general review of facial clefts and found increased numbers of isolated cleft palate in north west Wales, although at that time, numbers were small. A later review using 10 years of CARIS data (1998-2007) confirmed this picture with higher than expected rates in Gwynedd. During 2009/10 the situation regarding clefts in North Wales was reviewed in partnership with Public Health Wales. Investigations to date, whilst confirming a slight excess of cases in Gwynedd, have not identified any specific area for public health action (Figure 12).

The findings will now be presented to Betsi Cadwaladr Health Board.

Figure 12: Proportion (%) of live and still births with isolated cleft palate (Q35), by Welsh Local Authorities, 1998–2008 with 95% CI



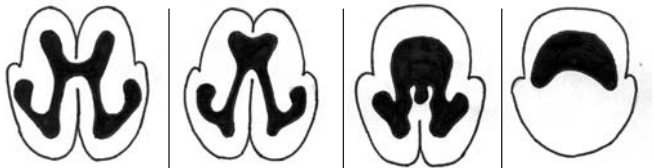
Facial Anomalies

Mid face syndromes

Holoprosencephaly

This complex anomaly results from a failure of the embryonic forebrain to divide to form the left and right halves of the brain, causing defects in the development of the face and in brain structure and function. The defect arises around the 6th to 7th week of gestation. The brain malformation can range from mild to severe and is classified below.

Figure 13: Holoprosencephaly: degree of severity

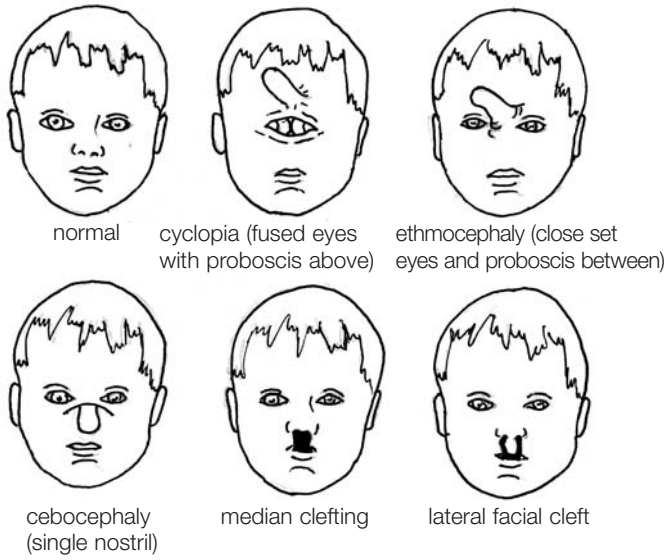


Normal	Lobar	Semilobar	Alobar
brain is divided; no abnormalities.	brain is divided; some mild abnormalities.	brain partially divided; moderate abnormalities with two hemispheres in the rear but undivided at the front.	brain is not divided; severe abnormalities.

With such serious anomalies the prognosis is poor and many women opt for a termination of pregnancy. Of those who choose to continue the pregnancy the perinatal mortality is high.

Isolated holoprosencephaly is rare and 28 cases were reported from 1998 to 2009, giving a gross rate of 0.7 per 10,000 total births) and most affected infants die within 6 months.

Figure 14: facial consequences of holoprosencephaly



Holoprosencephaly can be an isolated finding but may be associated with other anomalies including CVS, renal, gut and aneuploidies, particularly trisomy 13, trisomy 18 and triploidy.

Children can also have secondary conditions such as learning difficulties, epilepsy, diabetes insipidus, pituitary and hormone disorders, movement disorders and spasticity, gastroesophageal reflux, respiratory disorders, and hydrocephalus.

There is no cure and treatment is largely supportive or aimed at treating secondary conditions.

Ultrasound findings in holoprosencephaly

- Microcephaly and brachycephaly
- Absent cavum septum pellucidum
- Fused thalami
- Ventriculomegaly
- Monoventricle
- Incomplete cerebral mantle
- Facial abnormalities

Facial Anomalies

Septo-optic Dysplasia

This is a rare condition, similar to lobar holoprosencephaly, that causes blindness. The optic disc and the cavum septum pellucidum fail to develop. There also can be pituitary malfunction affecting growth, puberty and thyroid function. In 50% of cases there is schizencephaly (split brain).

CARIS reports 18 cases in the years 1998-2009, giving a gross rate of 0.5 per 10,000 total births.

Frontonasal Dysplasia

This mid-face syndrome is characterized by very widely set eyes (hypertelorism). The nose is broad with a tip that is often cleft. The lip may also have a median cleft.

Most cases are sporadic. In cases with no other anomalies the outlook is good. Craniofacial surgery can give good results.

The condition is extremely rare and CARIS reports 2 cases for 1998 to 2009.

Craniosynostosis

This describes premature fusion of the sutures of the skull. It has been discussed in detail in the 2008 report.

Certain syndromes associated with craniosynostosis have facial features.

Table 8: Facial and other features associated with craniosynostosis syndromes

Syndrome	Facial and other key features	Intelligence
Apert syndrome autosomal dominant	Hypertelorism, prominent eyes, syndactyly	50% have learning difficulties
Carpenter syndrome autosomal recessive	High forehead, mid facial hypoplasia, polydactyly	Variable
Crouzon syndrome autosomal dominant	Hypertelorism, proptosis, beaked nose, possible clover leaf skull	Usually normal
Pfeiffer syndrome autosomal dominant	Clover leaf skull common, broad thumbs and big toes, syndactyly	Compromised
Saethre-Chotzen syndrome autosomal dominant	Hypertelorism, mid face hypoplasia, high flat forehead, small ears	Usually normal
Craniofrontal dysplasia X linked dominant	Hypertelorism, frontal bossing, syndactyly, females more severely affected	Usually normal

Psychological issues

Congenital eye and facial anomalies can have considerable psychological consequences for children and their families. Parental adjustment is known to be an important factor in helping the child cope and so parents and the child may need psychological support from the point of diagnosis.

Psychological issues at the very early stages may include adjusting to the diagnosis and possible issues of trauma and loss, as well as bonding between parent and child. Congenital eye and facial anomalies can interfere with bonding, perhaps due to difficulties with verbal and non-verbal communication and feeding difficulties. This bond between parent and child and the two-way process of communication is known to have a potential long term impact on the child's development, both cognitively and socially. Other difficulties may include coping with reactions and comments of other people, issues of blame and dealing with frequent hospital visits, admissions or surgery.

As the child gets older, self-image and self-esteem become important. Psychological support and intervention may be useful when starting school, coping with comments, questions and staring from others, social anxiety and potential bullying.

Adolescence brings the challenge of transition to secondary school, identity, interpersonal relationships and increasing independence including decision making challenges.

Across the ages, there may be psychological issues associated with the specific condition. These include pain and anxiety about interventions and other mental health concerns such as low mood and generalised anxiety.

The psychological impact of the condition on the whole family and siblings in particular, is important. For the sibling this may include time separated from parents as a result of hospital admissions, anxiety and concern about their brother or sister and having to cope with comments and sometimes bullying from peers.

Psychological support and intervention can be offered across the developmental stages. This might involve working with other professionals involved in the child's health and education. Preventative work with families can help to promote psychological wellbeing, as well as therapeutic work with individual children, families and groups.

Vanessa Hammond
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South Wales Cleft Lip and Palate Service,
Morriston Hospital, Swansea.

Appendix A: CARIS rates for some key anomalies (1998-2009)

Anomaly	ALL CASES		LIVEBORN CASES		PROPORTION
	number	Rate per 10,000 total births	Number of liveborn cases	Rate per 10,000 live births	% cases liveborn
Anencephaly	258	6.5	6	0.2	2%
Encephalocele	87	2.2	21	0.5	24%
Spina Bifida	296	7.5	61	1.6	21%
Hydrocephaly	376	9.5	178	4.5	47%
Cataracts	144	3.6	144	3.7	100%
Sensorineural deafness	479	12.1	479	12.2	100%
Congenital cystic adenomatoid malformation of lung	59	1.5	51	1.3	86%
Hypoplastic left heart syndrome	133	3.4	62	1.6	47%
Transposition of great vessels	157	4.0	125	3.2	80%
Ventricular septal defects	2,003	50.8	1,828	46.6	91%
Cleft lip with/without cleft palate	449	11.4	363	9.2	81%
Cleft palate	375	9.5	301	7.7	80%
Hypospadias	1,025	26.0	1,019	26.0	99%
Multicystic kidney	249	6.3	177	4.5	71%
Bilateral renal agenesis	63	1.6	2	0.1	3%
Gastroschisis	237	6.0	208	5.3	88%
Diaphragmatic hernia	154	3.9	106	2.7	69%
Craniosynostosis	232	5.9	213	5.4	92%
Limb reduction defects	408	10.3	242	6.2	59%
Dislocation/dysplasia of hip	793	20.1	787	20.0	99%
Cystic fibrosis	181	4.6	174	4.4	96%
Congenital hypothyroidism	246	6.2	246	6.3	100%
Trisomy 21 (Down syndrome)	868	22.0	405	10.3	47%
Trisomy 18 (Edwards syndrome)	238	6.0	47	1.2	20%
45 X, (Turner syndrome)	160	4.1	47	1.2	29%

Appendix B: CARIS Champions & Co-ordinators

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 / Pat Mason (Newtown)
Prince Charles	David Deekollu	Jonathan Rogers	Kindry Dennett
Royal Glamorgan	Jay Natarajan	Jonathan Pembridge	Nicola Ralph
Royal Gwent	Vera Antao	Anju Kumar	Tim Watkins
Singleton	Geraint Morris	Marsham Moselhi	Helen Jenkins / Valerie Vye
UHW	Jenny Calvert	Christine Connor	Danielle Richards
West Wales General	Gwyneth Owen	Roopam Goel	Anya Evans
Withybush	Devasettihalli Appana	Chris Overton	Amanda Taylor / Delma Thomas
Wrexham	Praveen Jauhari	Bid Kumar	Sue Yorwerth
Ysbyty Glan Clwyd	Ian Barnard	Maggie Armstrong	Jenny Roberts
Ysbyty Gwynedd	Mair Parry	(to be confirmed)	Jackie Stockton & Linda Williams