

**Neural Tube
Defects
1995**

West Midlands Congenital Anomaly Register



Neural Tube Defects 1995

Report of Incidence,
Detection and Outcome

West Midlands Congenital Anomaly Register

Neural Tube Defects 1995

A Report of Incidence, Detection and Outcome

Ann Tonks
Project Manager

Mike Wyldes
Consultant Obstetrician &
Gynaecologist

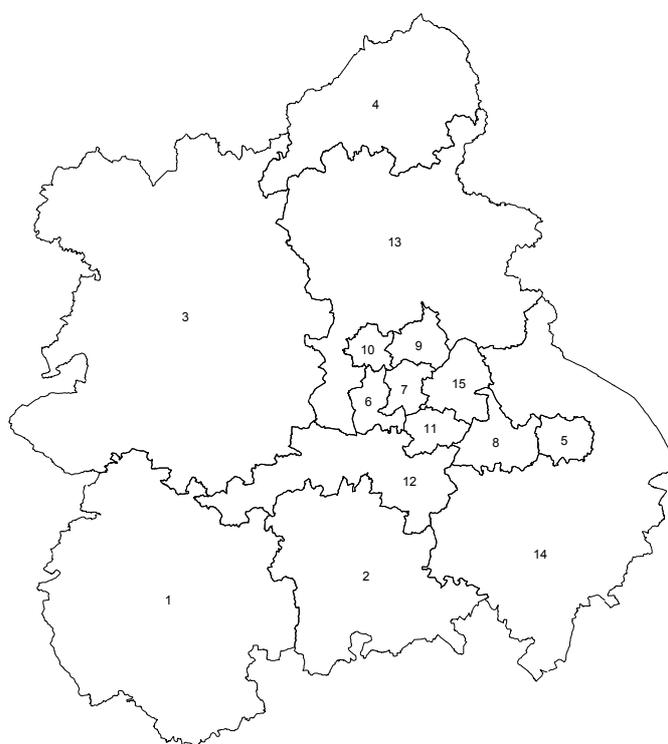
Martin Whittle
Professor of Fetal Medicine

West Midlands Perinatal Audit
Research Institute
Birmingham Heartlands Hospital
Bordesley Green East
BIRMINGHAM B9 5SS

Telephone: 0121-773 7736
Facsimile: 0121-773 7746
email: wmidlands@cesdi.org.uk

ISBN: 0 9523457 5 7

District Health Authorities in the West Midlands Region



KEY

- 1 HEREFORDSHIRE
- 2 WORCESTER
- 3 SHROPSHIRE
- 4 NORTH STAFFS
- 5 COVENTRY
- 6 DUDLEY
- 7 SANDWELL
- 8 SOLIHULL
- 9 WALSALL
- 10 WOLVERHAMPTON
- 11 SOUTH BHAM
- 12 NORTH WORCS
- 13 SOUTH STAFFS
- 14 WARWICKSHIRE
- 15 NORTH BHAM

Acknowledgements

The authors acknowledge with thanks the ultrasonographers, midwives, obstetricians, paediatricians and staff at the District Health Authorities within the West Midlands for supplying us with clinical information on anomaly cases.

Particular thanks to Donna Drinkall, the administrator of the West Midlands Congenital Anomaly Register for her hard work in collecting, validating, clinical coding and data-processing of all notifications received.

PREFACE

This report is the first formal feedback from the Regional Congenital Anomaly Register (CAR). The report summarises all data relating to cases of neural tube defect reported to the CAR that delivered during 1995, with some summary information relating to prenatal screening programmes. It gives comprehensive details of these cases, when and where the diagnosis was made and their outcomes.

The West Midlands Congenital Anomaly Register relies on notifications from health care professionals; sonographers, midwives, nurses and doctors. We believe that by encouraging multiple reporting from a number of different sources that the data held in the Congenital Anomaly Register are relatively complete and represent the best available information on this topic. The success or failure of the register rests upon the information received. We hope that by feeding back information on a regular basis we will not only help professionals in their work, but also will encourage continued and expanded use of the Register as a data source. This report aims to help the continual process of health care provision and commissioning.

Open neural tube defects are a major group of congenital anomalies. They include anencephaly, which is lethal, open spina bifida, which is usually associated with handicap, and encephalocele, which has a variable prognosis. These conditions occur because of a failure in the closure of the neural tube during organogenesis in early fetal life and are amenable to prenatal diagnosis by either maternal serum alpha-fetoprotein or ultrasound screening.

The report is presented in 2 parts. The first part deals with incidence rates for the West Midlands and its District Health Authorities. The second with detection and outcome of neural tube defect cases by maternity unit of delivery.

Mike Wylde
May 1997

TABLE OF CONTENTS

CLINICAL BACKGROUND OF NEURAL TUBE DEFECTS	2
DEVELOPMENTAL EMBRYOLOGY	2
PRENATAL DIAGNOSIS.....	2
<i>Maternal serum alphafetoprotein</i>	2
<i>Ultrasound scanning</i>	3
PAEDIATRIC MANAGEMENT	3
<i>Anencephaly</i>	3
<i>Spina bifida</i>	3
<i>Encephalocele</i>	3
METHODS.....	4
<i>West Midlands Congenital Anomaly Register</i>	4
<i>Reporting</i>	4
<i>Definition of neural tube defect</i>	4
<i>Denominators</i>	4
<i>Outcomes</i>	5
<i>Data Sources</i>	5
<i>Significance testing</i>	5
DEFINITIONS	6
RESULTS	7
<i>Ascertainment</i>	7
INCIDENCE RATES.....	8
ETHNICITY.....	9
FOLIC ACID SUPPLEMENTATION.....	10
DETECTION AND OUTCOME.....	11
INTRODUCTION	11
OUTCOME	12
PERINATAL MORTALITY	13
MULTIPLE PREGNANCIES.....	13
POSTMORTEM INVESTIGATIONS	13
PRENATAL DIAGNOSIS.....	14
METHOD OF FIRST DIAGNOSIS	16
RECOMMENDATIONS	17

CLINICAL BACKGROUND OF NEURAL TUBE DEFECTS

DEVELOPMENTAL EMBRYOLOGY

The spine and brain form early in fetal life, by differentiation and migration of tissue within the embryo. The structure that ultimately becomes the spine and head is called the neural tube. It starts as a groove along the back of the embryo at 16 to 18 days after fertilisation, around the time of the first missed period.

The edges of the groove rise and join to form the neural tube over the following 7 to 10 days. The neural tube joins first in the middle of the embryo, and closure continues from this position down towards the bottom of the "back", and up towards the top of the "head".

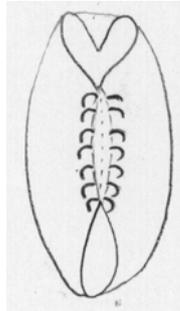


Figure 1
Closure of the neural tube

The most common defect in the formation of the neural tube is a failure of closure, either at the bottom (spina bifida) or top (anencephaly), like a zip that does not reach the end and leaves a gap.

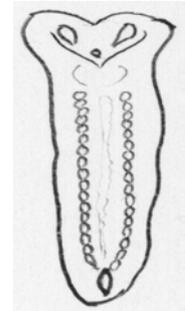


Figure 2
Failure of closure

The most severe defects are likely to be lethal early in fetal life, and will end in miscarriage, often without being recognised as fetal anomalies.

Anencephaly is often lethal during pregnancy, while spina bifida is more likely to result in a live birth, and is often compatible with survival, although associated with varying degrees of handicap.

Encephalocele is a condition in which the central nervous system (CNS) herniates through a defect in the surrounding structures, usually, but not always, in the midline. This may contain cerebrospinal fluid (CSF) only or a varying amount of brain or spinal tissue. The prognosis depends on the size of the lesion, and associated CNS dysfunction.

Neural tube defects are severe malformations because of the early stage in fetal life in which they occur. Often the initial event precipitates a string of other problems that ultimately lead to death or severe handicap. These include neuronal migration defects causing mental retardation and behavioural problems, and disturbance in the flow of CSF causing cerebellar abnormalities and frequently hydrocephalus.

PRENATAL DIAGNOSIS

Maternal serum alfafetoprotein

Historically the first method of prenatal screening was based on maternal serum alfafetoprotein (AFP) measurement, followed by amniocentesis and estimation of liquor AFP. AFP makes up much of the fetal blood protein at 16 weeks, and is raised in situations where blood protein can leak out from the fetus into the liquor. This is usually prevented by the fetal skin, and therefore any open defects (not covered with skin) may be identified in this way. Amniocentesis has now been superseded by ultrasound in making the diagnosis of a neural tube defect. This is because this method removes the potential risk of miscarriage associated with an invasive technique.

Ultrasound scanning

Ultrasound scanning is highly effective as a screening tool when offered to women at 18 to 20 weeks gestation. Anencephaly is possible to diagnose at a gestation of 12 to 14 weeks, by direct visualisation of the cranium. Spina bifida is most often diagnosed using the cranial signs of an abnormal shape of the fetal skull (lemon shape) and flattening and loss of the median sulcus in the cerebellum (banana shape). Hydrocephalus is often associated with spina bifida and the spine itself can be examined to demonstrate failure of closure of the vertebral arches, lack of skin cover and herniation.

PAEDIATRIC MANAGEMENT

Many neural tube defect cases will be correctly identified by prenatal diagnosis and the pregnancy terminated but inevitably some affected children will be born, either because of missed diagnosis or parental choice. Paediatric care of such cases is often complex and difficult, involving careful assessment, attempts at prediction of the likely outcome and intervention in some circumstances.

Anencephaly

The outcome for anencephaly is highly predictable and universally poor, making surgical intervention inappropriate. The care of these babies and their families is modelled on the care offered in other situations of terminal care. Symptomatic rather than curative treatment is appropriate for the baby. Parents need information, skilled counselling and support, which should start prenatally if a diagnosis is made.

Spina bifida

Open spina bifida, however, is more problematic, with some cases having a good outcome, while others have severe disability. The assessment of these cases relies upon careful examination of the lesion itself to identify sites of potential entry of infection; sensory and motor assessment of the lower limbs, bowel and bladder; assessment of the central nervous system and a full discussion with the parents. The options are either early surgical closure, with or without shunting of hydrocephalus or waiting for a time to allow the lesion to heal by granulation. The general principle of the early care of these children is to reduce disability in cases most likely to survive, but not to intervene aggressively to avoid death in children where the quality of life is likely to be low. These judgements are some of the most difficult made by doctors, and the importance of both personal experience and published information related to the outcome of these cases cannot be overstated.

Encephalocele

Encephalocele is similar to spina bifida in the variety of outcomes. Associated structural anomalies are relatively common, particularly renal anomalies, and need to be considered before other interventions are planned. Small lesions containing little or no brain substance will tend to have a good prognosis.

METHODS

West Midlands Congenital Anomaly Register

The West Midlands Congenital Anomaly Register (CAR) was set up in June 1994 and is administered by the West Midlands Perinatal Audit. The register aims to collect information on suspected and confirmed congenital anomalies, detected before and after birth from conception to outcome, up to the first 2 years of life. A number of minor anomalies are excluded from the register and these include sacral dimples and spina bifida occulta.

Reporting

Notifications are received by 2 methods. The first method is a notification card (Appendix A), which is used to notify the register of suspected anomalies. The card includes details of the type of anomaly and the estimated date of delivery and is most often completed by ultrasound departments. The second method is through a notification form (Appendix B), which contains much of the data set used for the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) but has additional details relating to the date that the anomaly is first suspected and the final postnatal diagnosis. The notification forms are usually completed by midwives, obstetricians and paediatricians.

The Congenital Anomaly Register is maintained on the same database as the register of CESDI notifications of fetal and infant deaths. In this way the number infants with lethal fetal anomalies can be validated. All anomalies are coded using the International Classification of Disease version 10 (ICD 10).

Additional information is also received from cytogenetics laboratories and Departments of Public Health. Inpatient episode data of infants with anomalies are also received from hospital information departments. These extra data are matched to the existing notifications to give estimated level of ascertainment, and additional clinical information is added in some cases.

Definition of neural tube defect

Cases of neural tube defect are defined here as those with anomalies coded to the ICD 10 codes Q00 (anencephaly and similar malformations), Q01 (encephalocele) or Q05 (spina bifida). Two cases of chromosome anomaly (both Edward's syndrome) with structural malformations including a neural tube defect are excluded from analysis in this report.

Denominators

The numerator comprises reported cases of neural tube defect. The denominator includes the numerator plus all babies who had any possibility of having a neural tube defect. As the number of cases of neural tube defect is small, the use of denominators in calculating incidence rates provides us with inter-district comparisons. Comprehensive clinical information is available for cases of fetal anomaly, however similar denominator data on all births are relatively difficult to obtain.

The appropriate denominator for calculating incidence rates is the total number of deliveries regardless of gestation but this information is unavailable. This report uses instead the sum of the number of births (live and stillborn), the number of terminations of pregnancy for fetal anomaly (<24 weeks) and any late fetal losses notified to the West Midlands Perinatal Audit. The denominator should also include all fetal losses under 24 weeks, however this information is not available. The numerator for incidence rates also includes cases of fetal loss due to neural tube defect.

Outcomes

This report divides outcomes of pregnancy into the following groups:

- Late fetal loss less than 24 weeks (LFL),
- Stillbirth 24 weeks or more (SB),
- Neonatal death under 28 days (NND),
- Postneonatal death 28 days up to 1 year of age (PNND),
- Alive.

Termination of pregnancy (TOP) is defined as a therapeutic termination undertaken under the 1967 Abortion Act, and excludes situations of induction following spontaneous fetal death in utero. Some terminations of pregnancy may result in a registerable stillbirth, or indeed a live birth regardless of gestation.

Data Sources

Numerator data (fetal anomalies)	West Midlands Congenital Anomaly Register
Denominator data (registerable births)	Office for National Statistics (ONS), and West Midlands' maternity units
Denominator data (fetal losses)	West Midlands Perinatal Audit
Townsend scores	West midlands NHS Health Executive
Ethnic group denominator data	1991 Census

Significance testing

All significance testing in this report is carried out by calculating the χ^2 statistic using 2 x 2 contingency (fourfold) tables. Yates's correction for continuity is incorporated into all χ^2 calculations. Significance is tested at a 95% confidence level i.e. $p < 0.05$ indicating a significant result. For small numbers, where an expected cell value is less than 5, Fisher's exact result is used.

DEFINITIONS

Denominators

The population at risk in the calculation of rate or ratio.

Early neonatal death

Death during the first week of life, 0-7 completed days (on or before the 7th day of life, 0-6 days 23 hours 59 minutes).

Late fetal losses

For CESDI a late fetal loss is defined as a spontaneous abortion (miscarriage) occurring from 20 weeks 0 days (140 days) up to the end of 23 weeks 6 days (167 days). If gestation is unknown or uncertain, birthweights of 300 grams or above are reported.

Neonatal death

Death during the first 28 days of life, 0-28 completed days (on or before the 28th day of life, 0-27 days 23 hours 59 minutes).

Perinatal mortality rate

The number of stillbirths and early neonatal deaths (i.e. those occurring in the first week) during a stated year per 1,000 live and stillbirths occurring in the same year.

Post neonatal death

Death between 1 month and 1 year of age (28 days and over, up to just before 1st birthday).

Registerable births/deaths

Births or deaths that must be legally notified to the Registrar for Birth and Deaths include all those delivered after 24 completed weeks of pregnancy, and all live births.

Stillbirth

Legal definition England & Wales.

“A child which has issued forth from its mother after the 24th week of pregnancy and which did not at any time after being completely expelled from its mother breathe or show any other signs of life”.

RESULTS

The Congenital Anomaly Register was used to identify 107 cases of neural tube defect with a date of delivery during 1995. These cases fall into one or both of two cohorts. The first group is West Midlands residents (n=102) and the second group is deliveries in West Midlands maternity units (n=106).

Ascertainment

The Office for National Statistics (ONS) operates a register of congenital anomalies called the Congenital Anomaly System. The primary purpose of the ONS register is not to estimate incidence at birth but instead to detect changes in the frequency of reporting groups of malformations. Until 1994 the ONS Congenital Anomaly System included only those malformations detected within 10 days of birth, this time limit no longer exists. The Congenital Anomaly System does not include data on terminations due to fetal anomaly. Both notification systems are voluntary.

To establish ascertainment levels a case matching exercise was performed with notifications to the ONS Congenital Anomaly System and the Congenital Anomaly Register for West Midlands residents born during 1995. When comparison between the 2 registers is restricted to registerable births, the ONS system has 21 cases of neural tube defect and the CAR has 30 cases for West Midlands residents.

The CAR matched 19 of the 21 ONS cases with its own. The 2 cases of neural tube defect identified by the ONS system only, are both recorded on the Congenital Anomaly Register; however neither is coded as a neural tube defect. The first was a suspected case of meningocele, but the postmortem revealed the anomaly to be "a fluid filled sac on the back involving skin only". The other case was a suspected meningocele with a postnatal diagnosis of nuchal congenital infantile fibrosarcoma.

When the 2 cases described above are excluded, 19 of the 30 CAR cases are held on the ONS system (1.6 times the number). If the number of neural tube defect cases is not restricted to registerable births, the CAR has 102 cases, 5.4 times the number registered with ONS.

In cases of neural tube defect, where malformations are detected early and prognosis is poor, a system that under-reports terminations of pregnancy is inappropriate for monitoring incidence rates. There is currently no national source of anomaly data that includes prenatally diagnosed cases that are subsequently terminated.

INCIDENCE RATES

Table 1 - Neural tube defect incidence by district of residence

District	Anencephaly			Spina bifida			Encephalocele			Total			Births
	n	rate	O/E	n	rate	O/E	n	rate	O/E	n	rate	O/E	
Herefordshire	1	5.3	0.78	1	5.3	0.78	0	0.0	0.00	2	10.6	0.71	1,890
Worcester & District	5	16.6	2.46	3	10.0	1.48	0	0.0	0.00	8	26.6	1.77	3,006
Shropshire	1	2.0	0.29	3	6.0	0.88	1	2.0	0.90	5	9.9	0.66	5,037
North Staffordshire	1	1.8	0.27	6	11.1	1.64	0	0.0	0.00	7	12.9	0.86	5,421
Coventry	2	4.9	0.73	1	2.5	0.37	1	2.5	1.12	4	9.9	0.66	4,042
Dudley	1	2.5	0.37	3	7.6	1.12	0	0.0	0.00	4	10.1	0.67	3,954
Sandwell	0	0.0	0.00	6	14.6	2.16	5	12.2	†5.53	10	24.4	1.63	4,101
Solihull	0	0.0	0.00	2	8.6	1.27	1	4.3	1.95	3	12.9	0.86	2,325
Walsall	1	2.8	0.42	3	8.4	1.25	1	2.8	1.28	5	14.1	0.94	3,552
Wolverhampton	6	18.8	†2.77	3	9.4	1.39	0	0.0	0.00	8	25.0	1.67	3,196
South Birmingham	6	10.0	1.48	1	1.7	0.25	2	3.3	1.51	9	15.0	1.00	6,011
North Worcs	4	11.8	1.75	2	5.9	0.87	0	0.0	0.00	5	14.8	0.98	3,384
South Staffordshire	4	5.7	0.85	4	5.7	0.85	1	1.4	0.65	9	12.9	0.86	6,979
Warwickshire	6	10.4	1.53	4	6.9	1.02	2	3.5	1.56	11	19.0	1.27	5,794
North Birmingham	8	8.6	1.27	4	4.3	0.64	1	1.1	0.49	12	12.9	0.86	9,300
Total	46	6.8	1.00	46	6.8	1.00	15	2.2	1.00	102	15.0	1.00	67,992

Table 2 - Neural tube defect incidence by maternity unit of delivery

Rate: rate per 10,000 births
O/E: observed rate/regional rate

* significantly lower rate than West Midlands expected, p < 0.05
 † significantly higher rate than West Midlands expected, p < 0.05

Note: Cases with 2 different classifications of neural tube defect appear in each of the relevant subtotal columns but only once in the total column.

There were more cases of neural tube defect delivered in West Midlands maternity units than to West Midlands residents during 1995. The neural tube defect incidence rate was 15.0 per 10,000 births to West Midlands residents, and 15.1 per 10,000 births in West Midlands maternity units. This is double the rate reported nationally¹ for 1994 (7.4 per 10,000 registered births). We think the reason for this is under-

¹ Murphy M, Seagroatt V, Hey K, O'Donnell M, Godden M, Jones N, Botting B. Neural tube defects 1974-94 -down but not out. *Archives of Disease in Childhood* 1996; **75**:F133-134.

reporting to the national register, particularly with regard to terminations. There were a similar number of cases with anencephaly and spina bifida, with incidence rates for both diagnoses of 6.8 per 10,000 births.

In Table 1 Worcester, Sandwell, Wolverhampton and Warwickshire residents had incidence rates for all neural tube defects above that which is expected regionally, however none of these rates reach significance.

Higher than expected numbers of neural tube defects are seen in births at Birmingham Women's, City, George Eliot, New Cross, Queen's, Ronkswood, Solihull, St. Cross and Walsall Manor hospitals. None of these elevated incidence rates reach significance.

The number of cases of anencephaly in Wolverhampton residents and cases of encephalocele in Sandwell residents was significantly higher than expected, as were the incidence rates seen for cases of anencephaly delivered at New Cross and Ronkswood hospitals. The rate at New Cross hospital reflects that seen in Wolverhampton residents. No maternity unit had a neural tube defect incidence rate significantly higher than the regional expected.

The relatively small numbers of cases seen during one year in any one unit make it difficult to identify units with lower than expected numbers of cases. Trends in low incidence will require study over several years.

ETHNICITY

The Congenital Anomaly Register data relating to ethnic origin of the mother are collected in the same ethnic groups used by the Office for National Statistics. However some of the numerator data is incomplete and has been collected in several different ways.

Ethnic denominator data relating to the number of maternities in the West Midlands are not available. Therefore the denominator used in the following table is the number of females in the population aged 15 to 44 years of age, as recorded by the 1991 Census. The following analysis does not take into account variations in birth rate between ethnic groups. A higher birth rate than expected will lead to an increased observed rate in Table 3.

Table 3 - Maternal ethnic origin of neural tube defect pregnancies, West Midlands residents

Mother's ethnic origin	n	Total	rate	O/E
White	80	993,053	0.81	0.83
Black Caribbean	2	20,027	1.00	1.02
Black African	0	1,413	0.00	0.00
Black other	0	4,002	0.00	0.00
Indian	2	41,350	0.48	0.50
Pakistani	12	21,721	5.52	5.66
Bangladeshi	1	4,020	2.49	2.55
Chinese	0	2,834	0.00	0.00
Other Asian	0	3,370	0.00	0.00
Other	1	4,677	2.14	2.19
Unknown	9			
Total	107	1,096,467	0.98	1.00

The numbers of cases in each ethnic minority group are relatively small, but it would appear that an increased rate of neural tube defects may affect women of Pakistani origin. This requires verification and further study, before any specific actions are considered.

FOLIC ACID SUPPLEMENTATION

The incidence of neural tube defects may be affected by a number of factors:

- i) Failure to take preconceptual folate supplements. Evidence suggests that preconceptual and early pregnancy folate supplementation is effective in reducing the incidence of neural tube defects.
- ii) Other social and economic factors may be important in the levels of periconceptual folate. These will be multi-factorial including diet, possibly smoking habits and socioeconomic status.
- iii) Maternal weight. The incidence of neural tube defects may be increased in mothers of increased weight².

The Medical Research Council Vitamin Study³ concluded that folic acid reduces the risk of neural tube defects by 72%. The Department of Health⁴ recommended women to increase dietary folates and take folic acid supplementation before conception. The Health Education Authority is running the "Folic Acid Campaign" of public and professional education.

Locally, the results of a study of periconceptual folic acid supplementation of 762 women attending 3 maternity units Good Hope, Birmingham Women's and Heartlands Hospitals⁵ showed that less than 10% of women take folic acid supplements appropriately. Knowledge and use are associated with age and ethnic group.

² Shaw GM, Velie EM, Schaffer D. Risk of neural tube defect affected pregnancy among obese women. *Journal of the American Medical Association* 1996; **275** (14):1093-6.

³ Prevention of neural tube defects: results of the Medical Research Council vitamin study. *Lancet* 1991; **338**:131-137.

⁴ Folic Acid and the prevention of neural tube defect, report from an expert advisory group. *Department of Health* 1992.

⁵ Gillies A, McLeod S, Wilson S. Periconceptual Folic Acid Supplementation: Women's knowledge and haematological values in pregnancy. Unpublished.

DETECTION AND OUTCOME

INTRODUCTION

Programmes for the prenatal diagnosis of neural tube defects are well developed in the West Midlands. Two methods of screening are in use, often together. The first is maternal serum AFP screening performed at 16 to 20 weeks gestation, the second is ultrasound screening, which is widely performed at 16 to 22 weeks for this purpose.

AFP serum screening is thought to be more than 90% sensitive for anencephaly and 80% sensitive for open spina bifida. It is less effective for encephalocele, which is usually skin covered and therefore not amenable to this technique. The current estimates of uptake are between 60 and 90% in most populations.

Ultrasound is based on examination of the fetal head, particularly the shape of the skull and the appearance of the cerebellum. These two features together give more than 90% sensitivity for all neural tube defects and when combined with an examination of the fetal spine are virtually diagnostic tests, even when applied to the whole population. The vast majority of women will accept an ultrasound scan if this is offered to them as part of antenatal care, but this service is not yet universally available throughout the region.

The prenatal diagnosis of neural tube defects is an aspect of prenatal care that is heavily dependent on the policies of the hospital in which the mother is booking. This report suggests that there is a high probability of neural tube defects being identified by the currently used methods. The factors that may influence the ability to diagnose by ultrasound include:

i) Maternal weight

Ultrasound is known to be more difficult in women of increased weight, and this seems likely to reduce the sensitivity of ultrasound in making a positive diagnosis. The maternal serum AFP concentration may be affected by maternal weight, being lower in women of increased weight.

ii) Quality of ultrasound machines

Machines under 5 years of age are recommended for fetal anomaly screening.

III) Time devoted to ultrasound scanning

Experience and practice suggest that 15 to 20 minutes needs to be allowed for each scan to ensure high sensitivity for structural defects.

IV) Training of sonographers

All sonographers need to be adequately trained in fetal anomaly screening.

v) Late booking

Women presenting after 24 weeks gestation are not generally offered serum AFP screening, and those who have no antenatal care will not be assessed by ultrasound. These women will therefore have a markedly reduced chance of prenatal diagnosis. Although the precise aetiology of neural tube defects is unknown, it is likely that women who present late in pregnancy will come from a higher risk group, and are unlikely to have taken preconceptual folate supplements.

This section of the report is analysed by maternity unit of delivery, rather than district of residence, because the issues relating to prenatal diagnosis tend to be specific to the provision of the service rather than the district of residence.

OUTCOME

Table 4 - Outcome of neural tube defect pregnancy by maternity unit of delivery

A termination of pregnancy can occur at any gestation following the diagnosis of a neural tube defect and results in either a late fetal loss, a stillbirth or a neonatal death. Table 4 shows that 84 (79.2%) of 106 cases of neural tube defect were terminated, 77 of the 84 terminations (91.7%) ending in a non-registerable birth.

There were 9 cases of stillbirth, 3 of these were late terminations of pregnancy (≥ 24 weeks gestation). Of the 7 neonatal deaths, 4 followed terminations and 2 of these were before 24 weeks gestation and if no life signs had been recorded would be defined as late fetal losses.

Table 5 - Outcome of pregnancy by classification of neural tube defect

Outcome	Anencephaly	Spina bifida	Encephalocele	Total
Late fetal loss				0
Late fetal loss - TOP	38	33	9	77
Stillbirth	5	2		6
Stillbirth - TOP		1	2	3
Neonatal death	2	1		3
Neonatal death - TOP	2	2		4
Post neonatal death		2	1	3
Alive		7	4	10
Total	47	48	16	106

Note: Cases with 2 different classifications of neural tube defect appear in each of the relevant subtotal columns but only once in the total column.

Table 5 shows that anencephaly has a universally poor outcome with 40 of the 47 cases being terminated and those not terminated ending in stillbirth or neonatal death. Spina bifida and encephalocele have a more variable outcome. Of those cases not terminated, 7 of the 12 with spina bifida and 4 of the 5 with encephalocele were alive at 1 year.

PERINATAL MORTALITY

The majority of the cases terminated would inevitably have ended in perinatal death. The decision to terminate therefore reduces the overall perinatal mortality rate in the West Midlands region by approximately 50 cases (assuming two thirds of these cases would end in perinatal death without intervention). This number of deaths would represent an increase in the perinatal mortality rate from 10.1 to 10.8 per 1,000 births in 1995.

The actual perinatal mortality rate attributable to neural tube defects in West Midlands births is low, 0.23 per 1,000 registerable births (16 in 69,795). The potential to reduce perinatal mortality by either reducing the incidence, or increasing the prenatal diagnosis rate further is therefore small. The prenatal diagnosis of neural tube defects already has a major impact on perinatal mortality from this cause.

In addition to the effect on perinatal mortality the reduction in morbidity from these conditions needs to be considered. The precise effect cannot be quantified, but a considerable reduction seems evident from these figures.

MULTIPLE PREGNANCIES

There were 2 cases of anencephaly in twin pregnancies, with no reported fetal anomalies in the unaffected twin. Both cases were diagnosed prenatally by ultrasound after 24 weeks gestation. One ended in stillbirth and the other as a neonatal death, the unaffected twin in both pregnancies was born alive.

POSTMORTEM INVESTIGATIONS

Table 6 - Postmortem examination of neural tube defect deaths

Outcome	Postmortem performed	Not requested	No permission	Total	% total
Late fetal loss				0	0.0%
Late fetal loss - TOP	64	6	7	77	83.1%
Stillbirth	2	1	3	6	33.3%
Stillbirth - TOP	2		1	3	66.7%
Neonatal death		2	1	3	0.0%
Neonatal death - TOP	2	1	1	4	50.0%
Post neonatal death	1	2		3	33.3%
Total	71	12	13	96	74.0%

Table 6 shows the proportion of the cases having postmortem examination. The frequency of postmortem consent seems to be related to the gestation at delivery. Parents having terminations before 24 weeks were the most likely to give consent (83.1%) and those where the baby died after 28 days were least likely (33.3%).

Late fetal losses following termination of pregnancy who had histological investigations are counted in the "postmortem performed" column.

PRENATAL DIAGNOSIS

Table 7 - Prenatal diagnosis of neural tube defects by maternity unit of delivery

Table 7 shows the number of prenatal diagnoses made by hospital of delivery. The number of diagnoses made or not made will depend critically upon the screening policies in place for detection of neural tube defects and the uptake of these services by pregnant women. The gestation at booking; the uptake of serum screening; the uptake of ultrasound scanning; the gestation at ultrasound scanning; the age of the ultrasound machines; the time allowed for each ultrasound scan and the training of the ultrasonographers are the key variables in the assessment of these programmes.

The prenatal diagnosis of neural tube defects is ideally undertaken before 24 weeks gestation. Table 7 shows that 85 (80.2%) of the 106 cases were correctly diagnosed before this time. A further 10 cases (9.4%) were diagnosed correctly between 24 weeks and delivery. Eleven cases (10.4%) were assumed to have remained undiagnosed before delivery as no record of a prenatal diagnosis exists in the Congenital Anomaly Register.

The cases not diagnosed before delivery were residents of 8 districts; 3 from Sandwell; 2 from Worcester and 1 case each from Shropshire, Coventry, Dudley, Solihull, Walsall and Warwickshire District Health Authorities.

Table 8 - Prenatal diagnosis of neural tube defects by outcome

Outcome	Diagnosed < 24 weeks	Diagnosed > 24 weeks	No prenatal diagnosis	Total
Late fetal loss				0
Late fetal loss - TOP	77			77
Stillbirth	4	2		6
Stillbirth - TOP	1	2		3
Neonatal death		2	1	3
Neonatal death - TOP	2	2		4
Post neonatal death			3	3
Alive	1	2	7	10
Total	85	10	11	106

The diagnosis of a neural tube defect usually results in a termination of pregnancy. Table 8 shows that of the 95 cases that were diagnosed prenatally, 84 (79.2%) were terminated although 7 of these (8.3%) resulted in a registerable birth.

When the diagnosis was made before 24 weeks, 80 of the 85 cases (94.1%) opted for termination. Two cases showed signs of life and are classified as neonatal deaths and 1 case was identified after 24 weeks making this a registerable stillbirth. There were 5 cases where a prenatal diagnosis was made before 24 weeks in which the parents elected to continue with the pregnancy, 4 ended in stillbirth and 1 was alive at 1 year of age.

The reasons for continuing with a pregnancy are complex and beyond the scope of this report, but there are parents who feel for a number of reasons that they should not terminate the pregnancy. The possible reasons include; the possibility of misdiagnosis; a feeling of not having the right to intervene to terminate the pregnancy; a belief that the mother is doing her best for the fetus or wanting to have a short time with the child despite the outcome.

Diagnosis of neural tube defects beyond 24 weeks gestation, which occurred in 4 of 10 cases (40.0%), was much less likely to lead to termination of the pregnancy. Of the 6 cases that continued 2 were stillborn, 2 were neonatal deaths and 2 were alive at 1 year of age. Failure of prenatal diagnosis occurred in 11 cases (10.4%) and 7 of these were alive at the time of reporting.

Prenatal diagnoses were known to have been made in 3 of 10 cases who survived for more than one year. One of the surviving cases was known to have undergone a successful surgical intervention to close a lumbosacral myelomeningocele.

Of the 3 spontaneous neonatal deaths, 1 case was diagnosed at 25 weeks but the parents elected to continue the pregnancy, 1 case was unidentified until delivery, and the third was a twin pregnancy, with one anencephalic fetus diagnosed at 30 weeks, 4 days before delivery.

Of the 3 cases of postneonatal deaths, all had no prenatal diagnosis. These cases survived for 29, 105 and 135 days, the last case having surgery for the closure of an encephalocele.

METHOD OF FIRST DIAGNOSIS

Table 9 - Reported primary positive screening method by classification of neural tube defect

Method of diagnosis	Anencephaly	Spina bifida	Encephalocele	Total
AFP	4	12	0	16
USS <16 weeks	13	3	3	17
USS 16-19 weeks	22	12	3	36
USS 20-23 weeks	2	11	3	16
USS > 23 weeks	5	4	3	10
at delivery	1	6	4	11
Total	47	48	16	106

Note: Cases with 2 classifications of neural tube defect appear in each of the relevant subtotal columns but only once in the total column.

Table 9 shows the primary positive screening method for neural tube defects. Maternal serum AFP was reported as raised in 16 cases. Ultrasound was the most commonly reported initial positive screening method, with a total of 79 cases, the majority before 24 weeks gestation. The register will tend to have a bias towards ultrasound reports, because the tendency is to report diagnoses rather than positive screening results such as high AFP values which are frequently not associated with fetal anomaly. There were no reported cases of amniocentesis being used for diagnosis following raised AFP.

Figure 3 - Gestation at ultrasound diagnosis

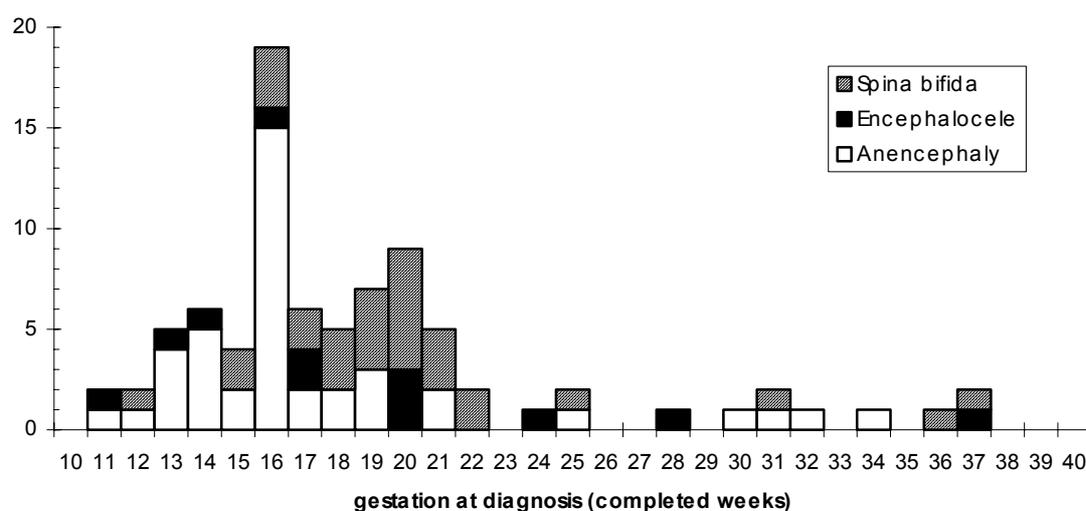


Figure 3 illustrates the timing of diagnosis of the 3 groups of neural tube defect, and shows that anencephaly tends to be diagnosed early in pregnancy, with the peak gestation of identification at 16 weeks, and some diagnoses made as early as 11 weeks. Spina bifida, however, has a peak gestation of identification at 20 weeks, perhaps reflecting the timing of the routine mid-trimester fetal anomaly scan.

The diagnoses after 24 weeks gestation are likely to represent a combination of late bookers and pregnancy complications arising from the neural tube defect, and are scattered throughout the pregnancy. These cases are relatively rare, compared with those in the mid-trimester.

Eighteen cases were referred to the Regional Fetal Medicine Centre for confirmation. No false positive diagnoses were made prenatally within the West Midlands region.

RECOMMENDATIONS

1. PERICONCEPTIONAL CARE

- 1.1 All women should be encouraged to take folate 400 µg for 3 months before conception and for the first 12 weeks of pregnancy⁶.

2. ANTENATAL CARE

- 2.1 Folate supplementation is documented in the pregnancy health records of all women at booking. This is preferable to asking women after a diagnosis of neural tube defect and may help to improve health education in the general population.
- 2.2 Women should be encouraged to book early enough to consider having either serum alphafetoprotein (AFP) or ultrasound for screening for neural tube defects.
- 2.3 Each maternity unit should have a screening policy for neural tube defects, either based on maternal AFP or fetal anomaly scanning.
- 2.4 Maternal serum AFP, when used, should be performed at or after ultrasound scans to establish the gestational age. Serum should be taken between 16 and 22 weeks gestation.
- 2.5 Each hospital should have in place a foolproof system for acting upon positive results, with rapid access to a specialised counsellor and diagnostic ultrasound facilities.
- 2.6 A screening programme using ultrasound should be based on spending 15 to 20 minutes of scanning time per patient. Ultrasound machines should be less than 5 years old. All sonographers should be well trained and have rapid access to knowledgeable counselling and support from medical staff.
- 2.7 Ultrasound screening should be organised within a department designed for obstetric ultrasound scanning. The diagnosis of a neural tube defect needs to be made positively, usually by 2 independent observers, since this diagnosis will usually lead to termination of pregnancy.
- 2.8 Each maternity unit should have a written policy for the diagnosis and further management of cases of suspected neural tube defect. This should include explicit standards for the confirmation of suspected cases, counselling of the parents and support during the continuing pregnancy or termination, whichever the couple chose.
- 2.9 The risk of chromosome anomaly in cases of isolated neural tube defect is small⁷. If karyotyping is thought to be clinically indicated, consideration should be given to obtaining tissue prenatally by amniocentesis, placental biopsy or fetal blood sampling, even when a termination of the pregnancy is to be undertaken, because there is a high chance of culture failure following delivery.

⁶ Prevention of neural tube defects: results of the Medical Research Council vitamin study. *Lancet* 1991; **338**:131-137.

⁷ Chen CP, Liu FF, Jan SW, Wang KG, Lan CC. Prenatal diagnosis of partial monosomy 13q associated with occipital encephalocele in a fetus. *Prenatal Diagnosis* 1996; **16(7)**:664-6.

3. INTRAPARTUM CARE

- 3.1 Every obstetrician must be aware of the guidelines of the Royal College of Obstetricians and Gynaecologists relating to termination of pregnancy for fetal anomalies, including the need to consider fetocide when the pregnancy is more than 21 weeks gestation.
- 3.2 If termination of pregnancy is offered and accepted, consideration should be given to the use of mifepristone, which significantly reduces the length of labour in mid-trimester termination.
- 3.3 Parents should be offered postmortem examination to confirm the ultrasound findings and identify any co-existing anomalies.

4. GENERAL

- 4.1 The West Midlands Congenital Anomaly Register continues to act as a focus for data collection during pregnancy, the neonatal period and the first 2 years of life.
- 4.2 Improved denominator data related to maternities must be collected to allow accurate analysis of different sub-groups.

Appendix A - Congenital Anomaly Register Notification Card

Appendix B - Congenital Anomaly Register Notification Form

Published by the West Midlands Perinatal Audit

ISBN: 0 9523457 5 7