OBJECTIVES

When you have completed this unit you should be able to:

1. Define a birth defect.
2. Calculate the prevalence of birth defects.
3. Give the mortality rate for birth defects.
4. List the causes of birth defects.
5. Understand chromosomal inheritance.
6. Understand the inheritance of single genes.
7. Define a teratogen and know their dangers.
8. Define a multifactorial birth defect.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way, nor may copies of the complete Programme be made, without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, however, parts of the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme are believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.

ISBN 0 7992 2254 2
51-1 WHAT IS A BIRTH DEFECT?

A birth defect is an abnormality of structure or function in a person, which is present from birth. The birth defect may be clinically obvious at birth, or may only be diagnosed sometime later in life. For example, a neural tube defect is a structural defect which is obvious at birth while haemophilia, which is also present at birth, is a functional defect that may only become obvious and be diagnosed when the child is older. Birth defects often present as an abnormal appearance or failure to grow and develop normally.

**A BIRTH DEFECT IS A DISORDER WHICH IS PRESENT FROM BIRTH**

Congenital disorder is another term that has the same meaning and definition as birth defect. Congenital means “present at birth”.

**Malformations** are the commonest form of birth defect. Malformations develop during the first trimester and are caused by failure of the embryo to develop normally. This results in a birth defect of one or more organs (e.g. heart, eye, brain).

*** An individual with an abnormal appearance is said to be “dysmorphic”. It is important to differentiate dysmorphic features from the normal range of features found in a family or community.

51-2 DO ALL BIRTH DEFECTS CAUSE DISABILITY?

No. Birth defects may be mild or serious. A mild defect may cause no disability. However, a person with a serious birth defect may die soon after birth, or survive with a disability due to the direct effect of the birth defect (e.g. neural tube defect) or due to a secondary effect (e.g. joint damage resulting from bleeding in haemophilia). Some serious birth defects can be treated and this may be life-saving or prevent serious disability.

Birth defects can cause a wide range of disability, e.g. physical disability, intellectual disability, blindness, deafness and epilepsy.

**SERIOUS BIRTH DEFECTS CAN CAUSE DEATH OR DISABILITY**

51-3 HOW IS THE FREQUENCY OF BIRTH DEFECTS MEASURED?

The frequency of birth defects (i.e. how common are individuals with a birth defect) is expressed as prevalence and birth prevalence:

1. The population prevalence is defined as the number of affected individuals per 1000 in a given population, e.g. 10 defects/1000 people.
2. The birth prevalence is defined as the number of affected infants per 1000 live births, e.g. 2 defects/1000 live births.

51-4 HOW COMMON ARE BIRTH DEFECTS?

At birth two to three percent of live newborn infants can be recognised as having a birth defect, i.e. the recognisable birth prevalence for all defects is 20-30/1000 live births in the first week of life.
However not all birth defects are diagnosed at or around birth, and by five years of age between five and eight percent of children are considered to have suffered the effects of a birth defect, i.e. a birth prevalence of 50-80/1000 live births. In some developing countries the birth prevalence of birth defects reaches 80/1000 children.

**THE BIRTH PREVALENCE OF BIRTH DEFECTS IS 50 TO 80 PER 1000 LIVE BIRTHS IN DEVELOPING COUNTRIES**

---

### Research done in rural Limpopo province, South Africa

Examining newborn infants on day one of life recorded a birth prevalence of serious defects of 15/1000 live births (1.5% of live births). Birth defects can be diagnosed at any age from the newborn period through to adulthood. Examples of birth defects that can present for the first time in adulthood include inherited cancers, Huntington disease and adult onset polycystic kidney disease.

**51-5 IF BIRTH DEFECTS ARE SO COMMON WHY ARE THEY NOT SEEN MORE FREQUENTLY AT CLINICS?**

1. Infants and children with serious birth defects are very likely to die when they are young, especially if there are inadequate medical services available for their care. Therefore they do not live long enough to be seen at clinics.
2. Many birth defects are not recognised and diagnosed.
3. It is often not realised that many of the conditions seen in clinics and hospital have a congenital origin, e.g. many forms of intellectual disability, cerebral palsy, deafness and blindness. Up to 50% of these conditions may be due to birth defects.

Therefore both the birth prevalence and population prevalence of birth defects in developing countries may seem to be much lower than it really is.

---

### Another reason why infants and children with birth defects are not seen is that their parents do not take them to hospital or clinic because they feel that they will not receive adequate attention or care, and the visit will be an unjustified burden on their limited family resources.

Experience from Limpopo showed that when genetic clinics were established, the population soon got to know and parents brought their children with birth defects.

**51-6 HOW MANY CHILDREN DIE FROM BIRTH DEFECTS?**

In South Africa about 1 million infants are born annually. Based on the available evidence, about 60 000 infants are born each year with a severe birth defect. Of these infants, about 25% will die in the first five years of life. Of all the infants who die in the first year of life, about 25% of deaths are due to serious birth defects.

It is estimated that 7.8 million children are born in the world each year with a serious birth defect. Of these children, at least 7.3 million (93%) are born in developing countries.

---

### It is quoted as a general rule that in industrialised countries 30% of children with serious birth defect will die in infancy (the first year of life), 30% will live with disability even if treatment is available, and 40% can largely be cured (mainly by surgery). Similar figures for developing countries are not available, but the number that die or are successfully treated will depend on the level of available health care. Currently at least 3.3 million children with a serious birth defect die annually.

---

**BIRTH DEFECTS ARE AN IMPORTANT CAUSE OF DEATH IN BOTH INFANCY AND CHILDHOOD**

---

**PERINATAL EDUCATION PROGRAMME**
CAUSES OF BIRTH DEFECTS

51-7 WHAT ARE THE CAUSES OF BIRTH DEFECTS?

Birth defects are caused by:

1. **Problems that are present before conception** (about 40% of birth defects) -
   (i) Chromosome disorders.
   (ii) Single gene defects.
   (iii) Multifactorial disorders.

   These are also known as genetic causes of birth defects.

2. **Problems occurring after conception** (about 10% of birth defects) -
   (i) Teratogens.
   (ii) Constraint.

   These are non genetic causes of birth defects. Note that all birth defects are not due to genetic causes.

3. **Cause not yet known** (about 50% of birth defects).

   *** The percentages given above are for industrialised countries. Figures for developing countries are not available.

---

THE CAUSE OF ABOUT 50% OF BIRTH DEFECTS IS NOT YET KNOWN

---

CHROMOSOMAL INHERITANCE

51-8 WHAT ARE CHROMOSOMES?

Chromosomes are packages of DNA (deoxyribonucleic acid) in which a person’s genetic plan of all their inherited characteristics are stored. Human cells have 46 chromosomes that are contained in the nucleus of the cell.

The chromosomes are paired (23 pairs), with 22 pairs called autosomes and one pair of sex chromosomes. Each pair of autosomes looks the same. The pair of sex chromosomes do not look the same because the X chromosome is longer than the Y chromosome.

Females have two X chromosomes (i.e. XX) while males have one X and one Y chromosome (i.e. XY). Like the 22 autosomes, the pair of X chromosomes in females look alike.

A picture of the 46 chromosomes is called a karyotype. The normal female karyotype can be written as 46,XX and the normal male karyotype as 46,XY. Each pair of autosomes is given a number (1 to 22).

---

A PICTURE OF THE CHROMOSOMES OF AN INDIVIDUAL IS CALLED A KARYOTYPE

*** In some textbooks, 46,XY is still written as 46 XY. 46,XY is preferable.
51-9  HOW ARE CHROMOSOMES INHERITED?

One chromosome of each pair of chromosomes is inherited from one parent and the other chromosome from the other parent. Therefore, both the mother and father give one chromosome to each pair of chromosomes found in the child. Half of the inheritance plan of each individual is inherited from the mother and the other half from the father. This is called sexual reproduction. An infant’s genetic plan is, therefore, inherited from both parents. This is why the inherited characteristics of the parents are shared in the child, and the child has features of both parents.

When the ova (female eggs) are produced in the mother’s ovaries, and the sperms (male eggs) in the father’s testicles, 46 chromosomes divide with only one copy of the plan in each ovum or sperm. The ova and sperms (also called gametes or sex cells), therefore, only have 23 chromosomes each. With fertilisation, a sperm and an ovum unite and combine their chromosomes to form the zygote (the first cell which will eventually develop into the fetus). The zygote has 46 chromosomes, half from the mother and half from the father. The zygote multiplies and grows to become an embryo (with cells developing into different organs). The embryo develops into the fetus (with formed organs) which, after delivery, is called the newborn infant.

**EACH PARENT GIVES ONE CHROMOSOME TO EACH OF THE 23 PAIRS OF CHROMOSOMES IN THE ZYGOTE**

PERINATAL EDUCATION PROGRAMME
Figure 51-2: The normal chromosome contribution of each parent.

*** All living organisms, plants and animals, have chromosomes. In humans the 46 chromosomes are known as the diploid number of chromosomes and the 23 chromosomes in the gametes as the haploid number. The process of cell division in which the gametes are formed and the number of chromosomes is halved (from 46 to 23) is called meiosis. After meiosis the ovum contains 22 autosomes and an X chromosome, and each sperm has 22 autosomes plus either an X or a Y chromosome.

Cell division in which the chromosome number stays the same can also occur (asexual reproduction) and this is called mitosis. This is the type of cell reproduction that occurs to make more cells so that the zygote can grow and develop into an embryo and fetus, and the body can grow or replace cells that die off during life.

51-10 WHAT ARE CHROMOSOME DISORDERS?

The process of reproduction (when the ova and sperm are made, fertilised and divide after conception) is not always perfect. Occasionally abnormalities occur in the chromosomes (the disorder is sporadic, i.e. the chromosome defect is due to chance). These chromosome disorders can result in:

1. An abnormal number of chromosomes in the cells -
   (i) Trisomy.
   (ii) Monosomy.
   (iii) Mosaicism.
2. **An abnormal structure of chromosomes in the cells** -

(i) Translocation.

(ii) Deletion.

If a whole chromosome or part of a chromosome is gained or lost in any of these processes, then the zygote that results will be abnormal as its genetic plan will have more or less genetic information than it should have. The embryo may abort spontaneously or result in an abnormal infant. Chromosomal disorders usually present with multiple abnormalities, including an abnormal appearance (dysmorphic features), developmental and growth delay and malformations. As most chromosomal abnormalities are not inherited, the risk of more than one child being affected (recurrence) is low.

---

**THE RISK OF THE SAME CHROMOSOME DISORDER OCCURRING MORE THAN ONCE IN A FAMILY IS SMALL**

51-11 WHAT ARE TRISOMY AND MONOSOMY?

This occurs when, during the formation of the gametes (ova or sperm), a pair of the parent’s chromosome does not split normally with one chromosome going to each gamete. Instead one gamete gets both the chromosomes, and therefore has 24 chromosomes, while the other gamete does not get a copy of that chromosome and, therefore, only has 22 chromosomes. This abnormal process of cell division, which results in two abnormal gametes, is known as non-disjunction.

When either of these two abnormal gametes fertilise with a normal gamete (containing 23 chromosomes) the resulting zygote will have either of the following:

1. An extra chromosome (trisomy) with 47 (i.e. 24+23) chromosomes in the cell.

2. One chromosome less (monosomy) with 45 (i.e. 22+23) chromosomes in the cell.

From an abnormal zygote with 47 chromosomes (trisomy) the fetus that develops will consist of cells which have 47 chromosomes. Similarly, for a zygote with 45 chromosomes (monosomy), where all the cells of the resulting fetus have 45 chromosomes.

---

**TRISOMY AND MONOSOMY ARE CAUSED BY NON-DISJUNCTION**
51-12 WHAT BIRTH DEFECTS ARE CAUSED BY TRISOMY AND MONOSOMY?

Many of the common chromosomal disorders (chromosomal birth defects) are caused by non-disjunction and the resulting trisomy or monosomy of different chromosomes. Most fetuses with trisomy and monosomy are not capable of living and result in early spontaneous abortion.

The chromosomes which can result in an infant being born and surviving with trisomy are 13, 18, 21, X and Y. The common trisomies are:

1. Trisomy 21 or Down syndrome (i.e. 47,XY+21 or 47,XX+21).
2. Trisomy 18 or Edward syndrome (i.e. 47,XY+18 or 47,XX+18).
3. Trisomy 13 or Patau syndrome (i.e. 47,XY+13 or 47,XX+13).
4. XXY in a male or Klinefelter syndrome (i.e. 47,XXY).
5. Trisomy X in a female (i.e. 47,XXX).
6. XYY in a male (i.e. 47,XYY).

The only chromosome that can be lost and result in a live born infant with monosomy is a sex chromosome X or Y. Therefore, the only monosomy seen is Turner syndrome (i.e. 45 XO).
**51-13 WHAT IS MOSAICISM?**

In the normal zygote there are 46 chromosomes. The zygote then begins dividing to form the embryo which contains many cells. This division of the one celled zygote results in a doubling of cells to 2, 4, 8, 16, 32 cells and so on, with all the cells having 46 chromosomes. However, in mosaicism, an error occurs. Early on in this dividing process one of the cells is involved in non-disjunction resulting in one cell having 47 chromosomes (trisomy) and the other cell only 45 chromosomes (monosomy). The monosomy cell usually dies but the trisomy cell may survive and divide. All future cells that come from it will be trisomy cells. Therefore, the embryo, fetus and infant that results will have some cells which are normal with 46 chromosomes and other cells which are abnormal with 47 chromosomes. This is called mosaicism.
As an example, if the non-disjunction was with chromosome 21 in a female then the infant would have some cells of 46,XX and others of 4, XX +21 resulting in mosaic Down syndrome (4, XX/47 XX +21). Mosaicism causes 1 to 2% of infants with Down syndrome. People with Turner syndrome can also be mosaic (46,XX/45X0).

*** Rarely, people are found with an extra piece of chromosome material that is called a marker chromosome. How this affects the person depends on what piece of chromosome is involved. Some people with marker chromosomes are normal, while others can have a chromosome disorder.

In the formation of gametes (ova or sperm), if none of the chromosome pairs divide, then 46 chromosomes will go to one gamete and none to the other gamete. If the gamete with 46 chromosomes becomes fertilised with a normal gamete with 23 chromosomes, the resulting zygote will have an extra set of chromosomes, i.e. 69 chromosomes (69,XXX or 69,XXY). This is called triploidy. It is also possible to have more than one extra set of chromosomes (polyploidy). Embryos with polyploidy usually abort spontaneously early in pregnancy. On the rare occasion when a triploidy (three sets of chromosomes) infant is born, it is very abnormal and either dies before delivery or very early in the neonatal period.

51-14 WHAT IS A CHROMOSOME TRANSLOCATION?

Translocation occurs when a piece of one chromosome breaks off and joins (translocates) on to another chromosome. If in this process no genetic material is lost or gained, this is called a “balanced” translocation and the person is clinically normal. However, if chromosome material is lost or gained then this is an “unbalanced translocation” and the person will be abnormal because their genetic plan has lost or gained genetic material.

Persons with balanced translocations are at risk of passing on the abnormal chromosomes to their offspring, resulting in abnormal embryos with unbalanced translocations. This can be the cause of recurrent spontaneous abortions. If the embryo survives the resulting infant will be abnormal. This risk varies according to the type of translocation.

51-15 WHAT IS A CHROMOSOME DELETION?

This occurs when a piece of a chromosome, big or small, is missing. There are several recognised syndromes in which a known piece of chromosome is missing. These include:

1. Prader Willi syndrome with deletion of a specific piece of chromosome 15.
2. Deletion 22 syndrome with deletion of a specific piece of chromosome 22.
3. Cri du chat (cry of a cat) syndrome with loss of the small arm of chromosome 5.

*** Sometimes a piece of chromosome copies itself and therefore the chromosome has two identical pieces of the chromosome and the genetic plan has extra chromosome material. This is called chromosomal duplication. There are recognised chromosome duplication syndromes, e.g. Cat Eye syndrome in which a piece of chromosome 22 is duplicated.

A piece of one end of a chromosome may come off (deleted) making it sticky. This end then sticks to the other end making a ‘ring’ chromosome. Because genetic material is lost from the one end of the chromosome in the process, the person usually has a chromosome disorder, often associated with growth failure and intellectual disability.
INHERITANCE OF SINGLE GENE DEFECTS

51-16 WHAT IS A GENE?

The genetic material on chromosomes is divided up into smaller packages of DNA called genes. Like chromosomes, genes occur in pairs, one gene from each parent. Together, each pair of genes usually determines a single inherited function by giving a set of instructions to the cell, such as a clinical feature (e.g. hair colour) or a single biochemical product (e.g. production of a protein or an enzyme). Genes make up the smallest parts of the genetic code. Children look like their parents because their genes are a mixture that is inherited from both mother and father. As this combination varies with each child, siblings look alike and yet have their differences. The only individuals with identical genes are identical twins.

A GENE IS A SMALL SECTION OF A CHROMOSOME AND CONTROLS A SINGLE FUNCTION. GENES OCCUR IN PAIRS, ONE BEING INHERITED FROM EACH PARENT

51-17 WHAT IS A SINGLE GENE DEFECT?

On the chromosomes, a person’s genetic plan is coded (“written”) in thousands of genes. Genes on the 22 autosomes and two X chromosomes always occur in pairs (alleles). One gene in each matching pair is inherited from the mother and the other gene in that pair is inherited from the father. Each pair of genes together codes for an inherited biochemical product (e.g. blood clotting factor) or clinical feature (e.g. eye colour) and gives the cell an instruction to carry out a particular activity. If the structure of the gene is abnormal, the instruction will also be abnormal and this may be harmful to the individual. An abnormal gene is called a single gene defect (i.e. there is a defect in only one gene).

A SINGLE GENE DEFECT IS AN ABNORMALITY IN ONE GENE

*** It is estimated that humans have between 30 000 and 40 000 pairs of genes. Over 6 000 single gene defects have been described.

51-18 HOW DO GENES BECOME ABNORMAL?

Almost all genes are normal and give the cell correct instructions. However, a gene can become abnormal by mutation. With a mutation, the DNA structure of a gene changes. Mutations are rare and may occur spontaneously or be caused by environmental factors, including radiation (solar radiation from the sun, nuclear radiation or excessive X-rays). These abnormal genes can be passed onto the next generation in the same way as normal genes are inherited. As a result, single gene defects are usually inherited (unlike chromosomal defects).

A MUTATION RESULTS IN A CHANGED GENE WHICH IS USUALLY ABNORMAL

*** In a mutation, the gene gives instructions for an incorrect sequence of amino acids and, therefore, an abnormal protein or enzyme is formed. A mutated gene may cause a clinical problem (e.g. haemophilia), a mild variant (e.g. red hair) or rarely a survival advantage.

51-19 WHAT TYPE OF GENES OCCUR?

A gene may be either a dominant or a recessive gene. Both dominant and recessive genes may be normal or abnormal.

GENES CAN BE EITHER DOMINANT OR RECESSIVE

PERINATAL EDUCATION PROGRAMME
51-20 WHAT IS A DOMINANT GENE?

In a pair of genes (alleles), the individual genes may be of different strengths, with the one being “stronger” and the other being “weaker”. The “stronger” gene dominates (overpowers) the “weaker” gene. Therefore, the “stronger” gene is called a dominant gene. The dominant gene controls the function of that gene pair (alleles).

If the dominant gene is abnormal, then the instructions sent from that gene pair will also be abnormal. As a result the cell may not function normally.

If the dominant gene is on one of the 22 autosomes, it is called an **autosomal dominant gene**. A clinical disorder caused by an autosomal dominant gene is called an **autosomal dominant disorder**. These conditions may be mild or severe but usually are not lethal (otherwise they probably would not be passed on to the next generation). Males and females are equally affected by autosomal dominant genes.

51-21 HOW ARE AUTOSOMAL DOMINANT GENES INHERITED?

If either the father or mother has an autosomal dominant gene, there is a **50% chance** of passing that gene on to each of their children. Both sons and daughters have an equal chance of inheriting an autosomal dominant gene.

**THERE IS A 50% CHANCE OF INHERITING A DOMINANT GENE FROM A PARENT**

If the autosomal dominant gene causes an abnormality of structure or function, the abnormality will be present in the parent with that gene, and also in each child that inherits that gene. Autosomal dominant disorders are, therefore, passed from one generation to the next. The effect of the abnormal gene will be present in both parent and child.

While most autosomal dominant genes are inherited, an autosomal dominant gene may also appear in a person for the first time as result of a new **mutation**. That gene will not be present in either parent. Therefore, the parents will be normal but the child will have the disorder. However, the new gene will be passed onto future generations in the same way as other autosomal dominant genes are inherited.
Figure 51-5: The pattern of autosomal dominant inheritance. There is a 50% chance that the autosomal dominant gene (e.g. D) will be passed from the affected parent to each child.

*** If both parents have the same dominant gene, there is a 75% chance (3 out of 4) that each child will inherit that gene. There is also a 25% chance (1 in 4) of inheriting both dominant genes, which is usually fatal if the dominant genes are abnormal. Therefore, all children will inherit either one or both dominant genes.

*** In a single family, some members will show all the clinical features caused by the dominant gene while others who inherit the gene may only show (express) some features. This is known as variable expression (e.g. neurofibromatosis). Some family members with a dominant gene may not show any features of that gene at all. This is called variable penetrance (e.g. polydactyly).

51-22 WHAT IS A RECESSIVE GENE?

If a dominant gene overpowers (suppresses) a “weaker” gene, the weaker gene is called a recessive gene. The dominant gene will control the function of that pair of genes. As a result, the instructions sent to the cell will be that of the dominant gene only. Therefore, the recessive gene will have no control over the cell and its effect will be “hidden” or suppressed.

A person is called a carrier if she/he carries a “hidden” recessive gene. In a carrier the effect of a recessive gene is not seen and the individual appears normal.
A person, who has both a dominant and a recessive gene (carrier), is said to be heterozygous for that pair of genes. If both genes are the same (both genes are dominant or both recessive), the person is said to be homozygous for that pair of genes. Only if both genes are recessive will they control that function of the cell. A recessive gene may be normal (e.g. result in blue eyes) or abnormal (e.g. result in oculocutaneous albinism). If both recessive genes are abnormal, that function of the cell will also be abnormal. A clinically normal carrier has both a normal (dominant) and an abnormal (recessive) gene for that feature.

A recessive gene on an autosome is called an autosomal recessive gene.

*** We all carry five to 10 abnormal recessive genes. As we are heterozygous for that gene (single dose), it generally has no effect on our health. Only if we are homozygous (double dose) for the same gene will we be clinically affected.

51-23 HOW ARE AUTOSOMAL RECESSIVE GENES INHERITED?

If both parents are carriers (i.e. they are heterozygous) for the same recessive gene, their children will have a 25% chance of inheriting the recessive gene from both mother and father (i.e. the child will be homozygous). Their children will also have a 50% chance of inheriting a recessive gene from only one parent to become a carrier (i.e. heterozygous). Getting the same recessive gene from both parents is commoner if the parents are closely related, e.g. siblings, cousins or an uncle and a niece (intermarriage or a consanguineous relationship), as they may inherit the same recessive gene from a common ancestor (e.g. grandparent).

With autosomal recessive inheritance, the parents and grandparents are usually normal and do not show the effect of the recessive gene. If a child inherits two abnormal autosomal recessive genes (i.e. one from each parent), they will have an autosomal recessive disorder. The risk of an autosomal recessive disorder is much higher if the parents are closely related.

The majority of single gene defects are autosomal recessive. Males and females are equally at risk of an autosomal recessive disorder.

If only one parent is heterozygous (a carrier), the children cannot be affected but they have a 50% risk of inheriting the recessive gene and, therefore, being a carrier.

**IF BOTH PARENTS ARE CARRIERS OF A RECESSIVE GENE, THERE IS A 25% CHANCE (1 IN 4) THAT THEIR CHILD WILL INHERIT BOTH RECESSIVE GENES**
Figure 51-6: The pattern of autosomal recessive inheritance. If both parents are heterozygous for a recessive gene (e.g. \( r \)), there is a 25% chance that a child will be homozygous and a 50% chance that a child will also be heterozygous for that gene.

**AUTOSOMAL RECESSIVE INHERITANCE**

*(BOTH PARENTS CARRIERS)*

- Carrier Father
- Carrier Mother
- R
- r

- Normal
- Carrier
- Carrier
- Affected

---

**51-24 WHAT IS X-LINKED RECESSIVE INHERITANCE?**

If a recessive gene is on an X chromosome, it is called an X-linked recessive gene (X-linked dominant genes and Y-linked genes are very rare).

X-linked recessive genes are inherited by girls in the same way as autosomal recessive genes. Girls have two X chromosomes and all the X-linked genes are in pairs. However, as the X and Y chromosomes are not identical (the Y chromosome is very short) the X-linked recessive genes in a male are not matched to a gene on the Y chromosome. Therefore, the X-linked gene, whether dominant or recessive, alone controls that function in males. As with autosomal recessive inheritance, mothers have a 50% chance (1 in 2) of passing her X-linked recessive gene to both her sons and daughters. However, it will only influence the function of the cell in her sons. It has no effect in her daughters as the gene is matched by a gene on the other X chromosome, inherited from the father.

Therefore, disorders caused by X-linked recessive genes are carried by females and affect males. Males have unaffected sons as they give them their Y and not their X chromosomes. However, there is a 100% chance that each daughter of an affected male will be a carrier.

Disorders caused by an X-linked recessive gene are called X-linked recessive disorders, e.g. colour blindness and haemophilia.

---

**X-LINKED RECESSIVE DISORDERS AFFECT MALES AND NOT FEMALES**
*** In males, an X-linked recessive gene acts as if it were a dominant gene as it is unopposed by the function of a matching gene. Females may have X-linked recessive disorders (e.g. colour blindness) if they inherit the same gene from both parents, i.e. both their X chromosomes carry the abnormal gene. Rarely, females who carry an X-linked gene may show mild signs of the disorder, e.g. haemophilia.

**X-LINKED RECESSIVE GENES ARE CARRIED BY MOTHERS AND AFFECT 50% OF THEIR SONS**

Figure 51-7: The pattern of X-linked recessive inheritance. There is a 50% chance that the recessive gene from the mother will be inherited by both sons and daughters. Only sons will be clinically affected as the X-linked recessive gene in daughters will be paired by a normal matching gene from the father.

51-25 WHAT ARE THE COMMON SINGLE GENE DISORDERS?

The most common autosomal dominant conditions are:

1. Polydactyly (extra digits).
Most common autosomal recessive conditions are found, or come from, tropical countries. They include:

1. Sickle cell anaemia.
2. Thalassaemia.
3. Oculocutaneous albinism.
4. Cystic fibrosis (the one autosomal recessive disorder that is common in people of European descent).

The most common X-linked recessive conditions are:

1. Red-green colour blindness.
2. Haemophilia.
3. Glucose-6-phosphate dehydrogenase deficiency (G6PD).

Some single gene disorders are often more common in particular populations or regions, e.g. sickle cell anaemia in West Africa, cystic fibrosis in Europe, thalassaemia in Mediterranean countries, polydactyly in black South Africans.

Figure 51-8: Examples of single gene disorders and their mode of inheritance.

<table>
<thead>
<tr>
<th>Autosomal dominant</th>
<th>Autosomal recessive</th>
<th>X-linked recessive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achondroplasia</td>
<td>Adrenogenital syndrome</td>
<td>Duchene muscular dystrophy</td>
</tr>
<tr>
<td>Apert syndrome</td>
<td>Congenital hypothyroidism</td>
<td>Fragile X syndrome</td>
</tr>
<tr>
<td>Crouzon syndrome</td>
<td>Cystic fibrosis</td>
<td>Glucose 6 phosphate dehydrogenase deficiency</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>Fanconi anaemia</td>
<td>Haemophilia</td>
</tr>
<tr>
<td>Huntington disease</td>
<td>Galactosaemia</td>
<td>Hunter syndrome</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>Oculocutaneous albinism</td>
<td>Incontinentia pigmenti</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>Phenylketonuria</td>
<td>Vitamin D resistant rickets</td>
</tr>
<tr>
<td>Polydactyly</td>
<td>Sickle cell anaemia</td>
<td></td>
</tr>
<tr>
<td>Treacher Collins syndrome</td>
<td>Spinal muscular atrophy</td>
<td></td>
</tr>
<tr>
<td>Tuberosus sclerosis</td>
<td>Tay Sachs disease</td>
<td></td>
</tr>
<tr>
<td><strong>Waardenburg syndrome</strong></td>
<td>Thalassaemia</td>
<td></td>
</tr>
</tbody>
</table>

Some conditions, such as polycystic kidneys, osteogenesis imperfecta, retinitis pigmentosa and mental retardation, may be inherited by more than one mode of inheritance, e.g. in some families as a dominant while in other families as a recessive disorder.

**51-26 WHAT IS A TERATOGEN?**

A teratogen is an environmental factor that can cause a birth defect. It can be a chemical substance like alcohol, an infection like the rubella virus (German measles) or a physical agent like X-rays. Teratogens interfere with normal development of the embryo usually early in pregnancy, but some can also damage the fetus later in pregnancy. If exposure to the teratogen is removed, there is little risk of a similar birth defect in a further child in that family. There are no genetic factors in birth defects caused by a teratogen.
51-27 WHEN DOES A TERATOGEN DO THE MOST DAMAGE?

The development of a baby from conception to birth is divided into three phases. The effect of teratogens is different in each of these phases:

1. **The pre-implantation phase**: (1-17 days post conception or 2 to 4 weeks after the start of the last menstrual period).

During this phase the fertilized egg (zygote) develops from one cell to a ball of many cells (the conceptus). This occurs while these cells are floating in a layer of fluid and moving from the fallopian tube into the uterus. At about 17 days post conception (4 weeks after the start of the last menstrual period) the conceptus begins to burrow into the lining of the uterus. Implantation and the development of the placenta and umbilical cord now begin.

Before implantation it is very difficult for a teratogen to get to the developing conceptus and damage it. In the unlikely event that a teratogen does damage the conceptus, it is so small and fragile that it would die. Implantation would not happen and the women would not even know she had conceived. Therefore, teratogens do NOT cause birth defects in the pre-implantation phase (1-17 days post conception or 2 to 4 weeks after the last menstrual period).

<table>
<thead>
<tr>
<th><strong>TERATOGENS DO NOT CAUSE BIRTH DEFECTS DURING THE PRE-IMPLANTATION PHASE OF DEVELOPMENT</strong></th>
</tr>
</thead>
</table>

2. **The embryonic phase**: (17-56 days post conception or 4-10 weeks after the start of the last menstrual period).

With implantation and the development of the placenta, the embryo and mother are in very close contact and a teratogen can now move easily from the mother through the placenta to the embryo. During this phase the organs of the body are developing, are very sensitive and are easily damaged by teratogens. Teratogens do the most damage in the embryonic phase. Structural birth defects that occur during the embryonic phase are called malformations, e.g. a cleft lip.

<table>
<thead>
<tr>
<th><strong>TERATOGENS CAUSE THE MOST DAMAGE IN THE EMBRYONIC PHASE OF DEVELOPMENT FROM 4 TO 10 WEEKS AFTER THE START OF THE LAST MENSTRUAL PERIOD</strong></th>
</tr>
</thead>
</table>

3. **The fetal phase**: (56 days after conception to birth or from 10 weeks after the start of the last menstrual period).

By 56 days after conception the embryo has turned into a fetus with fully formed organs. The fetus still needs to grow and mature before being born. Teratogens generally do little damage to the fetus in this phase of development, but there are some exceptions. For example, the fetal brain, which can be damaged more easily than other organs, can still be affected in this phase by some teratogens, particularly drugs like alcohol.

51-28 WHAT ARE EXAMPLES OF TERATOGENS?

1. **Maternal infections**:
   
   (i) Rubella virus.
   
   (ii) Cytomegalovirus (CMV).
   
   (iii) Toxoplasmosis.
   
   (iv) Herpes simplex virus.
   
   (v) Varicella virus (chicken pox and herpes zoster).
*** Toxoplasmosis, Rubella, Cytomegalovirus and Herpes are known as the TORCH organisms.

2. **Maternal illnesses:**
   (i) Diabetes mellitus.
   (ii) Epilepsy.

3. **Radiation in very large doses:**
   (i) Excessive amounts of X-ray.
   (ii) Nuclear radiation (e.g. Hiroshima).

4. **Drugs:**
   (i) Alcohol.
   (ii) Retinoic acid (for severe acne).
   (iii) Some antibiotics (e.g. tetracycline, streptomycin, thalidomide).
   (iv) Anti-cancer drugs (e.g. methotrexate).
   (v) Warfarin (an anticoagulant).
   (vi) Some anti-convulsants (e.g. phenytoin, valproic acid).
   (vii) Lithium (an antidepressant).

5. **Environmental pollutants:**
   (i) Methyl mercury.
   (ii) There are probably many more which have not yet been identified.

51-29 **WHAT ARE MULTIFACTORIAL BIRTH DEFECTS?**

These are birth defects that have a combined genetic and environmental cause. The environmental factor is often not known. The person affected with a multifactorial birth defect inherits a combination of genes from their parents that places them at an increased risk for a birth defect. If that individual then experiences certain environmental factors, the result will be a multifactorial birth defect. Multifactorial birth defects, therefore, require both genetic and environmental factors before they present. Neither the genetic factor nor the environmental factor alone will cause the birth defect. This is different from teratogens which cause birth defects without an obvious genetic factor. The risk that another child of the same parents will be affected by a multifactorial birth defects is small (about 5%).

Multifactorial birth defects are the commonest form of birth defect and usually affect a single structure, organ or system. They often present in infancy or childhood as malformations such as:

1. Neural tube defects and isolated hydrocephalus.
2. Clubfoot.
3. Cleft lip and/or palate.

**MULTIFACTORIAL BIRTH DEFECTS ARE USUALLY SINGLE WITH A LOW RISK OF RECURRENTNESS**

*** The risk of recurrence increases if more than one family member is affected.
51-30 WHAT IS CONSTRAINT?

External forces can result in birth defects after the fetus is normally formed (i.e. it is not a malformation). The cause of this type of birth defects is called constraint. There are two types of birth defects due to constraint:

1. Occasionally a normally formed fetus is pushed out of shape by mechanical force in the uterus (e.g. in multiple pregnancies, where there is little space in the uterus, or with oligohydramnios or large uterine fibroids). The head or chest may have an abnormal shape or the limbs may be bent. This type of birth defect is called a deformity. Deformities usually correct themselves after delivery once the pressure has been removed.

2. Sometimes a limb or other part of the body may be damaged by an amniotic band. A finger, toe or part of a limb may be amputated or have a constriction ring. The amniotic band results from a tear in the amnion early in pregnancy. This uncommon form of birth defect is called a disruption.

Birth defects may, therefore be divided into:

1. Malformations.
2. Deformations.
3. Disruptions.

Placing a birth defect into one of these three categories helps to identify the probable cause and timing of the defect.

CASE PROBLEMS

CASE 1.

A newborn infant at a district hospital is recognised as having a birth defect. The midwife comments that she very rarely sees birth defects. The doctor does not know the cause of the birth defect.

1. What is a birth defect?

It is an abnormality of function or structure in a person which is present from birth.

2. Why are birth defects rarely seen?

Because many birth defects are not recognised. A child may even die of a birth defect without the correct diagnosis being made. As a result, birth defects are commoner than they seem to be.

3. What is birth prevalence?

The birth prevalence of a birth defect is the number of infants born with that birth defect per 1000 liveborn infants. In contrast, the prevalence of a birth defect is the number of individuals with that defect per 1000 people in that population.
4. **What are the main known causes of a birth defect?**

Birth defects may be caused by:

(i) Problems at conception, such as chromosomal disorders, single gene defects or multifactorial disorders.
(ii) Problems after conception, such as teratogens or constraint.

5. **How often is a cause for a birth defect not found?**

About 50%.

6. **Are all birth defects due to genetic causes?**

No. Birth defects due to teratogens and constraint are not due to genetic causes. Therefore, they usually do not recur in the same family.

---

**CASE 2.**

An infant is brought to hospital with multiple abnormalities which were present at birth. The doctor thinks that the birth defects are due to a chromosomal abnormality. A blood sample is sent to a genetic laboratory. The report states that the infant has a trisomy.

1. **What is a chromosome?**

A chromosome is a package of DNA (a collection of genes) which makes up the genetic plan for the structure and functions of the body.

2. **Are multiple birth defects often due to chromosomal defects?**

Yes. Chromosomal defects usually cause multiple malformations including dysmorphic features, growth and developmental delay and malformations.

3. **What is a trisomy?**

With a trisomy the cells have three instead of two copies of a particular chromosome. For example, in Down syndrome due to trisomy, there are three instead of the normal two chromosomes 21.

4. **What is the cause of trisomy?**

Non-disjunction. During the formation of the gametes (egg or sperm), one gamete receives two chromosomes in error while the other gamete does not receive a chromosome (from that pair of chromosomes).

5. **Is trisomy the only way to get extra genetic material?**

No. With translocation a piece of one chromosome may be moved onto another chromosome. If the gamete gets the chromosome with the extra piece but not the chromosome that has lost a piece, that gamete will have extra genetic material.
CASE 3.

Parents with brown eyes have a son with blue eyes. The father asks the genetic nurse how brown eyed parents can have a blue eyed child.

1. **What determines the colour of a person’s eyes?**

A single pair of genes. The gene for brown eyes is a dominant gene while the gene for blue eyes in a recessive gene.

2. **Is the colour of a person’s eyes inherited?**

Yes. The colour of your eyes depends on the genes for eye colour carried by your parents.

3. **How can two brown eyed parents have a child with blue eyes?**

Because both parents are heterozygous (i.e. they each have one gene for brown eyes and another for blue eyes). If they both give their recessive gene (for blue eyes) to their child, that child will be homozygous for the blue eyed gene and, therefore, have blue eyes.

4. **What is the chance of their future children also having blue eyes?**

25%. This is the chance of being homozygous (having both genes recessive) if your parents are heterozygous. If one or both parents have two dominant genes for brown eyes, all their children will have brown eyes.

5. **Are recessive genes always abnormal?**

No. Many recessive genes (such as eye colour) are normal. However, recessive genes may be abnormal and, therefore, cause a clinical disorder.

CASE 4.

A young couple wants to get married. However the man has a serious birth defect which has been diagnosed as an autosomal dominant disorder. They ask their general practitioner what the chances are that their children will inherit the problem. The mention that they are cousins.

1. **What is an autosomal dominant disorder?**

It is a clinical problem caused by having an abnormal dominant genes on an autosome.

2. **What is an autosome?**

One of the 22 pairs of non-sex chromosomes. The X and Y chromosomes are not autosomes.

3. **What is a dominant disorder?**

It is a clinical condition caused by a dominant gene. A dominant gene is a “strong” gene that will overpower a recessive gene with which it is paired. The dominant gene will determine the effect that pair of genes has on the cell.

4. **What is the risk that their children will inherit their father’s abnormal autosomal dominant gene?**

50%. Therefore, the risk of having the same birth defect (disorder) is also 50%.
5. **Does it matter that they are cousins?**

This will not affect the risk of the children inheriting the autosomal dominant disorder. It would, however, increase the risk if both parents were carriers (heterozygous) for an abnormal recessive gene.

**CASE 5.**

Healthy parents of six children plan to have one last child. They have three normal daughters and one normal son. However, their other two sons both have a similar birth defect. The mother’s sister also has a son with the same birth defect. They want to know what the risk is of the planned child having the birth defect which is common in the family?

1. **What type of gene defect affects a number of children born to normal parents?**

The pattern of inheritance suggests a recessive gene (either autosomal or X-linked).

2. **Why are some of the boys and none of the girls affected?**

This may be due to chance. However, it strongly suggests an abnormal X-linked recessive gene defect. The fact that the mother’s sister also has an affected son indicates an abnormal gene carried by the females and affecting the males in the family.

3. **Which parent is probably a carrier of the abnormal gene?**

The mother.

4. **What is the risk of a further son being affected?**

50%.

5. **What is the risk of a further daughter being affected?**

Nil. However, she has a 50% chance of being a carrier.
OBJECTIVES

When you have completed this unit you should be able to:

1. Understand the care of people with birth defects.
2. Explain the principles of preventing birth defects.
3. Describe medical genetic screening.
4. Define genetic counselling.
5. List the goals, principles and process of genetic counselling.
6. Be an active listener.
7. Describe the normal reaction to loss.
8. Understand the implications of termination of pregnancy.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme is believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.

ISBN 0 7992 2253 4
MANAGEMENT OF BIRTH DEFECTS IN A COMMUNITY

52-1 HOW IS THE PROBLEM OF BIRTH DEFECTS MANAGED?

Managing the problem of birth defects requires the establishment of basic medical genetic services. The World Health Organisation has defined the aim of medical genetic services as helping people with a genetic disadvantage (i.e. those affected and those at risk of having a child with a birth defect) to live and reproduce as normally as possible.

Medical genetic services require management programmes for birth defects. These consist of a comprehensive plan to:

1. Provide the best possible care for people with birth defects, and for their families.

MEDICAL GENETIC SERVICES COMBINE THE BEST POSSIBLE PATIENT CARE WITH THE PREVENTION OF BIRTH DEFECTS

CARING FOR PEOPLE WITH BIRTH DEFECTS

52-2 WHAT CARE IS NEEDED FOR PEOPLE WITH BIRTH DEFECTS?

Caring for people with a birth defect involves three steps:

1. **Identify the birth defect:**

   A birth defect must be identified as early as possible to ensure the best response from treatment and genetic counselling. In low resource nations, primary health care providers should learn to diagnose their country’s common and important birth defects. In South Africa these would include:

   (i) Down syndrome.
   (ii) Oculocutaneous albinism.
   (iii) Waardenburg syndrome.
   (iv) Haemophilia
   (v) Fetal alcohol syndrome.
   (vi) Neural tube defects.

   A definite diagnosis cannot always be made. However, it remains important to know that the person has a birth defect and to recognise the disabilities that may be associated with the birth defect.

2. **Provide appropriate treatment:**

   Having identified a birth defect, the primary health care provider has the responsibility for offering and providing appropriate treatment. This may be available in the local clinic or hospital or may require the patient to be transferred to a regional centre. Whenever possible, treatment should be provided in the primary health care facility which is closest to the patient and the family's home.

3. **Offer genetic counselling and psychosocial support.**

   With treatment the affected person and family, especially parents, should be offered genetic counselling and psychosocial support. As far as possible, for common disorders, this should occur at a primary health care clinic or hospital. Counselling will help them understand and deal with the issues resulting from the birth defect.
52-3 CAN ALL PEOPLE WITH BIRTH DEFECTS BE OFFERED THE BEST POSSIBLE CARE?

Yes. The World Health Organisation (WHO), in its discussions on the development of medical genetic services, realised that levels of healthcare are different between countries, and even within different regions of a country. Therefore, what can be offered to patients in different circumstances varies, but in any situation “the best possible patient care” should be offered.

In no circumstance should care not be offered.

52-4 HOW CAN YOU IDENTIFY A BIRTH DEFECT AND MAKE A GENETIC DIAGNOSIS?

A birth defect is identified and, where possible, a genetic diagnosis is made in the same way as all medical diagnoses by:

1. **Take a full history:** This includes a presenting history, birth history, past history, social history and a family history. The family history must be recorded as a three generation family tree.

2. **Do a physical examination:** A full examination must be done. Many of the abnormal clinical signs (dysmorphic features) of birth defects are external and visible. These signs can be used to suggest a possible diagnosis. If a patient has three or more recognisable dysmorphic features or an obvious abnormality (e.g. cleft lip), this indicates a birth defect.

3. **Perform investigations:** Investigations relevant to each case can be ordered and the results obtained.

4. **Make a final diagnosis, if possible:** The diagnosis should be confirmed by a doctor, if possible, before treatment and genetic counselling are offered. If a final diagnosis cannot be reached, and this is holding back the on-going care of the patient, referral to an appropriate centre must be considered.

PEOPLE WITH A BIRTH DEFECT USUALLY HAVE THREE OR MORE RECOGNISABLE FEATURES OR AN OBVIOUS ABNORMALITY

52-5 WHAT IS A THREE GENERATION FAMILY TREE?

This is a graphic presentation (a pedigree) of a family, over at least three generations to help with the identification and method of inheritance of genetic defects. The three generation family tree is drawn after taking a careful family history. Normal individuals, people with birth defects, probable carriers (recessive or X-linked) and pregnancy losses are all plotted on the family tree.

Males are indicated with a square and females with a circle. An open square or circle is used for normal individuals and a completely filled in square or circle for affected individuals. A half filled in square or circle indicates autosomal recessive carriers (heterozygotes) while a circle with a dot in the centre represents a an X-linked female carrier. A diagonal line through a square or circle indicates that the person has died. One line is used for each generation. Parents are linked to each other with a horizontal line, while parents and children are linked with a vertical line. Two parallel lines link parents who are related (consanguineous).

PERINATAL EDUCATION PROGRAMME
Figure 52-1: A family tree of a female child with a birth defect, whose carrier parents are unaffected but consanguineous. Two grandparents and one great grandfather were also carriers. This family tree suggests an autosomal recessive pattern of inheritance.

52-6 CAN A MEDICAL GENETIC DIAGNOSIS ALWAYS BE MADE?

No. In about 50% of people with birth defects a definitive diagnosis cannot be made (e.g. the person has dysmorphic features that do not fit into a recognisable syndrome). They may present with a variety of problems including intellectual, physical, auditory (hearing) and visual (sight) disability and epilepsy. Early recognition of these disabilities is important for treatment and genetic counselling. Care must be given even if a final diagnosis cannot be made.

52-7 WHAT TREATMENT IS AVAILABLE FOR PEOPLE WITH BIRTH DEFECTS?

Three means of treatment for people with a birth defect are available. Many treatments cannot cure the problem, but they can improve the situation. Unfortunately, many of the latest treatment methods are expensive and not available in low resource countries, including South Africa.

1. **Medical treatment**: People with birth defects often have problems that can be treated with medication. Because of limited resources in developing countries, primary health care providers often have to give and monitor these medications, if necessary, in co-operation with specialists in secondary or tertiary care centres. Examples of medical treatment that can be undertaken in primary health care centres include antibiotics for recurrent infections, sunscreen for oculocutaneous albinism, cardiac failure treatment, blood transfusion for anaemia, factor VIII or IX for haemophilia and anti-convulsant medicines for epilepsy.

See Annexure A for a more complete list of care and prevention possibilities, including those possible in primary health care units in South Africa.

2. **Surgical treatment**: Surgery, especially paediatric surgery, often saves lives or offers significant improvement for many serious birth defects. At the primary health care level, people with these conditions need to be recognised early and affected individuals transferred to the appropriate surgical unit.

Examples include surgery for meningomyelocele, omphalocele and heart defects, orthopaedic manipulation and surgery for club foot, removal of congenital cataracts, and surgery for cleft lip and palate. The transfer of the patients with a birth defect, such as an omphalocele, needs to be carefully managed to ensure that the patient arrives in the best clinical condition possible.
3. **Neurodevelopmental therapy (NDT) and rehabilitation**: This should include the availability of occupational, speech and physiotherapy, and other therapies needed for rehabilitation, e.g. stoma therapy for individuals with repaired meningomyelocele who are incontinent. They assist people with birth defects to overcome their disabilities and to integrate into society to the greatest extent possible. In some developing countries, such as South Africa, where therapists are not always available, community based rehabilitation programmes can be developed to undertake this task and help people with disability live and function in their community.

4. **Genetic counselling and psychosocial support**: Genetic counselling and psychosocial support are a major part of caring for people with birth defects and their families.

### PREVENTION OF BIRTH DEFECTS

#### 52-8 HOW CAN BIRTH DEFECTS BE PREVENTED?

There are two practical approaches for the prevention of birth defects:

1. Basic reproductive health approaches to prevent birth defects.
2. Medical genetic (population) screening, prenatal diagnosis and genetic counselling.

#### 52-9 WHAT ARE BASIC REPRODUCTIVE HEALTH APPROACHES?

These are methods of preventing birth defects that ensure normal infants are conceived and the embryo and fetus are not damaged by teratogens or constraint during pregnancy. These methods need to be in place before conception and are dependent on community education. These methods are also referred to as ‘**primary prevention of birth defects**’ and are the preferred method for the prevention of birth defects. All countries should develop their medical services to include these methods of prevention of birth defects, which are mainly carried out in primary health care centres. They include:

1. Family planning.
2. Peri-conception care.

### BASIC REPRODUCTIVE HEALTH APPROACHES ARE METHODS AIMED AT THE PRIMARY PREVENTION OF BIRTH DEFECTS

#### 52-10 HOW CAN FAMILY PLANNING PREVENT BIRTH DEFECTS?

A functional, accessible family planning service that is well used by people is essential for the prevention of birth defects. If this service is available:

1. Women have the option of limiting their family size. As a result, fewer infants are planned and, therefore, fewer infants with birth defects are born.
2. Women of advanced maternal age (35 years or older) can reduce their the risk of having an infant with a chromosomal abnormality, particularly Down syndrome, as this risk increases as they get older. Family planning allows women the option of completing their families before 35 years of age.
3. Women, who have had a child with a birth defect that is inherited, are at risk in following pregnancies of having further affected children. With family planning they have the option of not having more children.
**52-11 WHAT IS PERI-CONCEPTION CARE?**

This is care of women’s health before conception and in early pregnancy (the first eight weeks). Peri-conception care of women’s health can prevent some birth defects.

Peri-conceptional care should include fathers in pregnancy preparation and care, and promote responsible fatherhood.

**52-12 WHAT PERI-CONCEPTION CARE CAN HELP TO PREVENT BIRTH DEFECTS?**

1. **Improve women’s diet:**

Birth defects can be caused by deficiencies of certain essential dietary nutrients (e.g. vitamins and minerals). Increasing the quantity of these nutrients in the diet can prevent certain birth defects. The best known example of a birth defects due to inadequate nutrients is fetal brain damage due to the mother’s diet being deficient in iodine. This can be prevented by adding iodine into the populations’ salt supply (fortification). In South Africa salt is fortified with iodine.

*** Yearly about 28 million infants worldwide are born at risk of mild intellectual disability, and 60 000 infants develop cretinism, due to inadequate amounts of iodine in the mother’s diet.

Folic acid is another example. Fortifying basic foods with folic acid, or giving folic acid as a pill (supplementation), for three months before and after conception significantly reduces the birth prevalence of neural tube defects. In South Africa, bread is fortified with folic acid, and maize meal will be fortified with folic acid in the near future.

Diet can also be improved by removing substances that can damage the embryo and fetus (teratogens). The best example is alcohol. Community education to warn women of reproductive age of the dangers of alcohol to the embryo and fetus is necessary.

**IMPROVING THE DIET OF WOMEN REDUCES THE RISK OF BIRTH DEFECTS**

2. **Avoiding and treating maternal infections:**

All children should be immunised against rubella (German measles) as rubella during early pregnancy causes serious birth defects.

3. **Detect and treat maternal health problems:**

Diabetes mellitus (IDDM) and epilepsy are maternal illnesses that can be detected before pregnancy and correctly treated, reducing the risk of birth defects. Avoid drugs which may damage the embryo or fetus (teratogens) such as warfarin, lithium and some anticonvulsants.

**PERICONCEPTIONAL CARE CAN PREVENT SOME BIRTH DEFECTS**

**MEDICAL GENETIC SCREENING**

**52-13 WHAT IS MEDICAL GENETIC SCREENING?**

Medical genetic (population) screening uses tests or questions in a population, to find people or pregnancies at increased risk of particular birth defects. When identified, these individuals can be offered further tests to confirm the diagnosis, or management to prevent or treat the condition. These people being screened, including pregnant mothers, will not have presented with complaints or signs of the disorder for which they are screened. Medical genetic screening can identify pregnant women at an increased risk of having an infant with a specific birth defect, e.g. Down syndrome. For other people it detects an increased risk for being affected by a particular birth defect, e.g. congenital hypothyroidism in infants.
MEDICAL GENETIC SCREENING IS A PROCESS UNDERTAKEN IN POPULATIONS TO IDENTIFY PEOPLE AT INCREASED RISK OF BEING AFFECTED BY, OR HAVING A CHILD WITH, A BIRTH DEFECT

52-14 WHEN CAN MEDICAL GENETIC SCREENING TESTS FOR BIRTH DEFECTS BE DONE?

1. **Pre-conception screening (Primary prevention):** This is the ideal form of screening and prevention as it allows the parents at risk the greatest range of reproductive choices.

2. **Antenatal screening (Secondary prevention):** This is done once pregnancy is confirmed, late in the first trimester or early in the second trimester. If medical genetic screening during pregnancy for a particular disorder is positive, then further testing may be needed to confirm or exclude the diagnosis (i.e. the prenatal diagnosis). The mother or couple should receive genetic counselling before they consider prenatal diagnosis and again once the result of the prenatal diagnosis is available, especially if the result confirms an abnormality.

3. **Postnatal screening (Tertiary prevention):** This is done after birth. Medical genetic screening is done in newborn infants, older children and adults. In the newborn period the most cost efficient means of screening is for every infant to be physically examined by a trained observer before discharge from hospital or clinic. For example, this will identify most infants with Down syndrome. Blood screening tests can also be done for certain conditions, e.g. congenital hypothyroidism.

*** Once an infant with a birth defect is born, tertiary prevention consists of early detection and diagnosis, treatment and genetic counselling to prevent, to the greatest extent possible, deterioration, complications, disability and dependency of the infant with the birth defect.

52-15 WHAT MEDICAL GENETIC SCREENING TESTS FOR BIRTH DEFECTS ARE AVAILABLE?

All medical genetic screening should be carried out with the full knowledge and understanding of the person being screened. There should be pretest and post test counselling.

1. **Pre-conception screening:**
   
   (i) Taking a family history.
   
   This is screening by asking questions. Taking and interpreting a three generation family history from women of reproductive age is an inexpensive way of identifying persons with an increased risk of having a child with a birth defect. This could be done in family planning clinics.

   (ii) Carrier (DNA) screening.
   
   Screening for carriers of common recessive single gene defects is carried out in countries with a high prevalence of these birth defects. The birth defects screened by blood tests include sickle cell anaemia, thalassaemia and cystic fibrosis. This is expensive and is only done in a few countries.

2. **Antenatal screening:**
   
   (i) Advanced maternal age screening to identify women 35 years of age and older.

   (ii) DNA carrier screening. This can also be carried out on parents during pregnancy, but it is preferable to do this before conception.

   (iii) Ultrasound screening. Ultrasound screening for Down syndrome can be offered from 11 to 14 weeks gestation and a scan for other congenital abnormalities between 18 and 23 weeks. Unfortunately, this is not generally available in South Africa due to the lack of necessary equipment and trained staff.
Maternal serum screening. Maternal serum can be tested for different chemicals early in the second trimester and the results used to calculate a risk for a fetus with Down syndrome (Triple test) and neural tube defects (alpha fetoprotein). This form of screening is not generally available in South Africa as accurate gestational ageing of the pregnancy with ultrasound is necessary for the tests to be done.

Rhesus blood group screening to identify Rh negative women who may have an infant with neonatal jaundice due to blood group incompatibility.

### 3. Postnatal screening:

(i) Clinical examination of the newborn infant before discharge from the clinic or hospital. Unfortunately, this is often not done routinely in South Africa.

(ii) Newborn screening on cord blood or heel prick blood, e.g. for congenital hypothyroidism. This is only available in a few centres in South Africa.

*** Several birth defects can be screened for using neonate’s blood from a heel prick, put on Guthrie cards (blotting paper). Birth defects that can be screened for in this manner include sickle cell anaemia, glucose-6-phosphate dehydrogenase deficiency and congenital hypothyroidism. This is not offered in South Africa yet.

### 52-16 WHY IS MEDICAL GENETIC SCREENING FOR BIRTH DEFECTS NOT AVAILABLE TO EVERYONE IN SOUTH AFRICA?

Medical genetic screening can be expensive and requires functioning health systems and infrastructure to be done correctly. Each country must decide on its priorities before establishing these screening services. In South Africa the only antenatal medical genetic screening that is offered to all the population is for Rhesus blood grouping and syphilis. Advanced maternal age screening could and should be offered. General examination of all newborn infants could also be easily offered.

### 52-17 WHAT CHOICES DOES A PREGNANT WOMAN HAVE IF SHE HAS AN INCREASED SCREENING RISK FOR A BIRTH DEFECT?

If a pregnant woman is shown by genetic screening to be at increased risk for having a fetus with a birth defect, she and her partner should receive careful genetic counselling regarding their specific situation and the options available to them.

This counselling will offer them two choices:

1. **To have prenatal diagnosis:** Prenatal pregnancy diagnosis can confirm whether the fetus does or does not have a birth defect. This may require invasive procedures such as amniocentesis to obtain fetal cells or amniotic fluid for testing. Amniocentesis involves inserting a thin needle under ultrasound guidance through the abdominal wall into the uterus. There is a small risk that the procedure will cause complications, including a miscarriage. This risk is about 1% with an experienced sonographer. The woman should be informed of this so she can include this information in her decision making process. In some circumstances, ultrasound examination can be used to make a prenatal diagnosis. An ultrasound examination is a non invasive procedure that can be very helpful in identifying structural abnormalities.

*** In specific circumstances fetal cells can also be obtained by chorionic villus (placental) biopsy or cordocentesis (drawing blood from the umbilical cord). Both have higher complication risks than amniocentesis and are only offered at a few tertiary centres in South Africa.

2. **To continue the pregnancy without prenatal diagnosis:** A pregnant woman may decide to take this choice, knowing and understanding the risks for having an infant with a birth defect.
Figure 52-2: Amniocentesis to obtain a sample of amniotic fluid.

GENETIC COUNSELLING

52-18 WHAT IS COUNSELLING?

Counselling is a process of education, communication and support by which a counsellor helps people to cope with difficult situations in their lives so that they are able to make important decisions and find realistic ways to solve their problems. Counselling, therefore, helps people to make their own choices and supports these decisions, rather than simply giving them advice and information or telling them what to do.

COUNSELLING IS ABOUT EMPOWERING PEOPLE TO MAKE IMPORTANT DECISIONS AND TO SOLVE THEIR OWN PROBLEMS

Counselling is further discussed in Unit 35 of the Perinatal HIV/AIDS manual of the Perinatal Education Programme.

52-19 WHAT IS A COUNSELLOR?

A counsellor is someone who is trained to educate, assist and give psychosocial support to people with problems. They offer relevant information and discuss options for people to manage their problems and better cope with their lives. This empowers peoples to make their own decisions and take the best course of action according to their personal circumstances, customs, and religious and moral beliefs.

52-20 WHAT IMPORTANT SKILLS ARE NEEDED FOR COUNSELLING?

Two essential skills are needed for counselling:

1. A good knowledge of the topic or situation being discussed.
2. The ability to communicate effectively. Communication is the basis of counselling.
52-21 WHAT IS EFFECTIVE COMMUNICATION?

Communication in counselling is a two-way process in which information, knowledge, thoughts and ideas are passed between the people being counselled and the counsellor. The spoken word is the most important means of communication but the counsellor must be aware that people may also pass important messages by showing their emotions and in their body language (how they act). The counsellor must learn to pick up these signs as it helps in gathering information and giving appropriate understanding (empathy) and emotional support. Effective communication requires the skill of active listening.

EFFECTIVE COMMUNICATION IS A COMBINATION OF ACTIVE LISTENING AND USING WORDS WITH CARE AND CONSIDERATION

52-22 WHAT IS ACTIVE LISTENING?

Active listening is the process of hearing not only the words people say, but also noting their body language and emotional reactions, and trying to understand the meaning behind their words and actions. In order to understand what a person is saying and to respond appropriately, the counsellor must become skilled in actively listening to people.

ACTIVE LISTENING IS THE KEY TO EFFECTIVE COUNSELLING

52-23 WHAT IS NEEDED FOR ACTIVE LISTENING?

A good listener should:

1. Put the person at ease so that they can feel free to talk.
2. Remove distractions and concentrate on what is being said. Close the door. Do not take phone calls, fiddle with notes or tap your pencil.
3. Not talk too much. You cannot listen if you keep talking. Be silent when silence is needed. Do not interrupt unnecessarily or finish peoples’ sentences.
4. Show interest.
5. Express empathy and understanding. Try to put yourself in their place so that you can see the problem from their point of view.
6. Help people being counselled to identify problems and then try to understand the causes before encourage them to develop ways of finding solutions.
7. Be patient and allow questions.

52-24 WHAT ARE COMMON ERRORS WHICH PREVENT ACTIVE LISTENING?

1. Talking more than listening.
2. Interrupting and arguing.
4. Concentrating only on facts, not feelings.

“IF YOU DO NOT LISTEN TO THE PERSON BEING COUNSELLED, DO NOT EXPECT THEM TO LISTEN TO YOU”

52-25 WHAT ELSE CAN HELP EFFECTIVE COMMUNICATION?

1. Choose your words carefully to ensure that what you say is what the person being counselled will understand.
2. Say what you mean and give simple messages.
3. Remember that as you can receive messages from the person being counselled from their body language, emotional reactions and tone of voice, so can you pass messages to them in the same way. Make sure you pass the “right” message.
4. Practice active listening.
5. Repeat important information and make sure it is understood.
52-26 WHAT CAN BLOCK EFFECTIVE COMMUNICATION?

Being judgmental, critical, threatening, manipulative, uninterested or trying to control the discussion.

“WORDS ARE LIKE MEDICATION, THEY HAVE THE ABILITY TO HEAL BUT THEIR SIDE EFFECTS CAN BE HARMFUL”

52-27 WHAT IS GENETIC COUNSELLING?

Genetic counselling is counselling which helps people with birth defects and their families make the most appropriate decisions and come to terms with the situation. It assists them in making choices regarding the care of the affected individual, future prevention of the condition, and its effect on the family. These decisions must be respected. Good genetic counselling should also provide the appropriate understanding, psychological (emotional) and social support necessary in these circumstances.

Genetic counselling helps people who are:

1. Affected by a birth defect.
2. At risk of inheriting a birth defect.
3. Passing on a birth defect to their children.
4. Carrying a fetus with a birth defect.

52-28 IN WHAT WAY CAN GENETIC COUNSELLING HELP PEOPLE?

Genetic counselling helps individuals or families with birth defects to understand:

1. The diagnosis (what is the problem).
2. The cause of the birth defect.
3. The method of transmission (inheritance).
4. The clinical effects, prognosis and available treatment.
5. The risks of recurrence.
6. The options for preventing the particular birth defect in future pregnancies.

52-29 WHAT ARE THE GOALS OF GENETIC COUNSELLING?

The main goals of genetic counselling can be remembered by using the word DIAS (i.e. an anagram). They are:

1. Define the problem:

Confirm a diagnosis, if possible, and identify those issues related to the diagnosis concern the counselled person or persons. Find out from the person or people being counselled what they expect and need from the genetic counselling.

2. Inform:

Tell the person or the people being counselled about the diagnosis, the prognosis, the available treatment, genetic risks (risk assessment) and the options for prevention in future pregnancies.
3. **Allow people to make their own decisions (Autonomous decision making):**

With the information available to them, the individuals or family should be encouraged to make their own decisions regarding their situation based on their personal circumstances, customs, religious and moral beliefs. These decisions must be accepted and respected by the genetic counsellor, nursing staff and medical team involved in their care.

4. **Support:**

During the genetic counselling process, and thereafter, individuals and family should receive the understanding (empathy), psychological (emotional) and social support they may need or request to enable them to make the necessary decisions and to adjust to their particular circumstances. This may require referring them to other professionals and social agencies.

52-30 **WHAT ARE THE PRINCIPLES OF GENETIC COUNSELLING?**

The counsellor has the responsibility for:

1. **Non-directive education:**

   The genetic counsellor must:
   
   (i) Have the appropriate information to do the counselling. If not, the counsellor should acquire this information or have the confidence to refer the person or people being counselled to someone with the knowledge.
   
   (ii) Make sure the person or people being counselled are fully informed. The counsellor must pass on all the knowledge he or she has on the topic under discussion, including the good and the bad aspects.
   
   (iii) Give the necessary information in a language, and at a level of understanding, that the person or people being counselled fully understand.
   
   (iv) Give the information to the person or people being counselled in a non-directive manner. This means the information is given in a way that must not influence their future decisions in the direction the counsellor would choose.

2. **Autonomy (able to decide for themselves):**

   The genetic counsellor must:
   
   (i) Ensure that each person being counselled must be allowed to make their own decisions. Their choices may be very different to that of the counsellor.
   
   (ii) Empower the persons being counselled to make their own decisions.
   
   (iii) Respect and accept these decisions, even if they would not be the option chosen by the counsellor, i.e. be non-judgemental. Reassure them that the medical team working with them will also respect and accept their decisions and make sure they continue to get proper care.

3. **Support:**

   The genetic counsellor must:
   
   (i) Encourage people being counselled to express their feelings and needs freely.
   
   (ii) Provide non-judgemental communication and support for the individual and family choices and encourage the medical and genetics management team do the same.
   
   (iii) Maintain confidentiality within the management team.
52-31 WHAT MUST BE KNOWN TO BE ABLE TO GIVE GENETIC COUNSELLING?

1. Who should receive genetic counselling?
2. The clinical details and natural history of the common birth defects, especially the defect on which the patient or parents are being counselled. This includes clinical features, prognosis, cause or mode of inheritance, available treatment and options for prevention.
3. How to obtain a detailed family history and construct a three-generation family tree.
4. How to use the family tree to decide on the mode of inheritance for the disorder in the family tree.
5. How to estimate simple genetic risks from a family tree.
6. The procedures (e.g. amniocentesis) and genetic tests for prenatal screening and diagnosis (e.g. chromosomal analysis) of common birth defects.
7. Basic counselling skills.
8. The local, provincial and national resources available for care of individuals with birth defects.
9. The parent support group facilities available locally, provincially and nationally.

52-32 WHAT ARE THE CHARACTERISTICS OF A GOOD GENETIC COUNSELLOR?

A good genetic counsellor should:

1. Be knowledgeable regarding the situation or disorder that is under discussion.
2. If not knowledgeable, they should be able to get the appropriate information, or have the confidence to refer the parents to someone who does have the information.
3. Be honest.
4. Have the courage to be able to say “I don’t know”. It is not possible to know everything you may need in a given situation. You can always find answers later or refer them to someone who will know.
5. Be a good listener and good communicator. This helps to build a relationship of trust and acceptance so that feelings can be expressed, even negative or bad ones.
6. Be respectful of the other person’s feelings and point of view, understanding that every person is an individual who will experience their problem in their own unique way.
7. Be non-judgemental (do not judge what is right and wrong or place blame).
8. Be relaxed and calm, i.e. controlled. A counsellor should not become emotionally involved with people receiving counselling.
9. Be non-directive. This means to give the people being counselled the necessary information they need, and the options they have, in a manner that does not influence, one way or the other, the decisions they have to make.
10. Be trustworthy and respectful of confidentiality.
11. Be able to “break bad news”.
12. Be able to support people through their problems, including the normal mourning (grieving) process associated with death or serious problems.
13. Be patient, caring and understanding.

52-33 WHAT ARE THE PHYSICAL REQUIREMENTS FOR GENETIC COUNSELLING?

1. A place with privacy and relative comfort to consult with the people being counselled. There should be as few interruptions as possible (telephones, cellphones, bleepers, noise and people coming in and out).
2. People being counselled and the counsellor should be able to sit reasonably close so that they can hear and interact with each other but not feel cramped or uncomfortable. Big desks form a barrier between the people involved and prevent easy interaction. Ideally counselling is a “round table conference”.
3. Enough time must be available for the counselling to fully cover the problems being discussed.

PERINATAL EDUCATION PROGRAMME
52-34 WHO SHOULD PROVIDE GENETIC COUNSELLING?

A doctor, genetic-trained nurse or genetic counsellor, provided they are competent and have received appropriate training.

Nursing staff, with appropriate training, have been found to be competent at providing genetic counselling in under-served areas in South Africa. Unfortunately, due to the lack of trained and experienced staff, people needing genetic counselling are often counselled by untrained or poorly trained people.

52-35 WHO NEEDS GENETIC COUNSELLING?

Any person who is affected by a birth defect, or at risk of inheriting a birth defect, or at risk of passing on a birth defect to their children.

These include:

1. People with a birth defect.
2. Parents of a fetus, infant or child with a birth defect.
3. Parents of an unexplained intrauterine, neonatal or infant death, if this was considered to be due to a birth defect.
4. People with a family history of a birth defect, who are considering having children.
5. Couples who are married to a relative, such as a cousin (consanguinity).
6. People diagnosed as carriers or at risk of being a carrier of a recessive genetic disorder, e.g. haemophilia or oculocutaneous albinism.
7. Couples diagnosed with an abnormal fetus on ultrasound examination.
8. Women who have had recurrent pregnancy losses (more than two miscarriages).
9. Pregnant women, or women who wish to have an infant, where the fetus is at risk of a birth defect because of fetal infection (e.g. rubella), maternal disorders (e.g. diabetes) or teratogens (e.g. alcohol).
10. Couples identified by antenatal screening who have an increased risk of a birth defect (e.g. advanced maternal age, abnormal ultrasound or a positive maternal serum screening test).

ANY PERSON WHO IS AFFECTED BY A BIRTH DEFECT, AT RISK OF INHERITING A BIRTH DEFECT, AT RISK OF PASSING ON A BIRTH DEFECT TO THEIR CHILDREN NEEDS GENETIC COUNSELLING

52-36 WHAT STEPS DOES A GENETIC COUNSELLOR FOLLOW IN PROVIDING GENETIC COUNSELLING?

1. **Gather information:**

   Obtain full medical details, including the presenting problems, birth, family, social and past history. It is important to find out whether the individual or family understands their problems and what they expect the genetic counselling session to achieve.

2. **Define the problem:**

   Identify the birth defect and try to obtain a definitive diagnosis if possible, using the above information and other sources, including genetic testing.

3. **Risk assessment:**

   This is necessary where individuals or families are concerned about themselves or future generations inheriting the particular birth defect. Simple genetic risk calculations can be made from a three-generation family tree, based on the type of inheritance of the condition.
4. **Educating:**

Using the above skills and information, the individual or family must be fully informed about:

(i) The diagnosis.
(ii) The cause and method of transmission (inheritance).
(iii) The consequences and prognosis and treatment, if this is available.
(iv) Options for prevention of their genetic condition in future pregnancies.

5. **Allow own (autonomous) decision making:**

(i) The individual or family are encouraged and allowed to make their own decisions regarding their problems.
(ii) This is done according to their personal circumstances, customs, religious and moral beliefs.
(iii) These decisions must be respected and accepted by the genetic counsellor, nursing staff and medical team involved in their care.

6. **Provide psychosocial support:**

(i) People should receive the understanding (empathy), psychological (emotional) and social support they may need or request.
(ii) This is required during the counselling session and may be ongoing afterwards.
(iii) Social support includes being able to help someone with a birth defect receive the necessary medical, educational, social or financial assistance that society can provide.
(iv) Genetic counsellors should know what resources are available and develop a local, provincial and national list of resources so that they can refer appropriately.

Note that there is an enormous difference between genetic counselling and simply providing information and advice.

See Annexure B of social grants available for individuals with birth defects in South Africa.

**52-37 WHY IS BREAKING BAD NEWS ABOUT BIRTH DEFECTS DIFFICULT?**

Giving people bad news about a birth defect will probably cause them great distress. They will have to face loss, including loss of life, health or the possibility of not having normal children. There are certain emotional responses that all people facing loss experience. A counsellor must understand these responses and be able to assist those grieving or mourning their loss.

**52-38 HOW DOES A GENETIC COUNSELLOR BREAK BAD NEWS?**

Genetic counsellors have to use their ability in effective communication to break bad news. Preparing for and breaking bad news is very important because the way this is done may greatly affect the response of the person receiving the news. The counsellor should therefore follow guidelines to try and ensure that this is done in the best possible manner. This should include:

1. Find a suitable environment for the counselling session.
2. Decide who should be in the counselling session and ensure everyone is politely introduced.
3. Establish from the person being counselled their knowledge and understanding of the situation under discussion. Also assess their general level of understanding and awareness so that your discussions will be at a level that is understandable.
4. If appropriate, assess through careful questioning how much the person wants to know.
5. Inform the person being counselled of the bad news. Do this carefully and gently, offering small amounts of information at any one time. When people receive bad news they often cannot take in too much information at a time.

6. Use simple language, leaving out medical terms they will not understand (e.g. trisomy 21 or tetralogy of Fallot) and use teaching aids (e.g. pictures) if necessary.

7. Every now and then check to see if they understand what is being told to them.

8. Be prepared and willing to repeat information one or more times.

9. Answer questions to the best of your ability, and never be afraid to say that you do not know. Answers can be found later or you can refer them to someone who will know.

10. Write down the main points or give them prepared written information about the birth defect so that they can read and think about the information later.

End the counselling session with an open invitation to those being counselled to contact the genetic counsellor with any further queries, need for psychosocial support or for further genetic counselling they require. Provide them with contact particulars.

52-39 HOW DO PEOPLE RESPOND TO LOSS?

People who suffer loss may go through a typical series of reactions. These are:

1. Denial:

   When faced with bad news involving loss, many people first refuse to believe what they have been told. This is their way of giving themselves time to begin to deal with and understand the terrible news that causes them to feel hopeless and helpless.

2. Anger:

   Once they realise the news is true; the next reaction may be anger, rage or resentment. This is often directed at other people including family members (e.g. wife or husband, father or mother), friends, medical or nursing staff and even God. It is a defence that people use to protect themselves against despair, and a genetic counsellor must understand this and support the person being counselled through this stage.

3. Bargaining:

   In this stage, which is usually short, people may try to enter into some sort of bargain with God, to try and reverse or put off feeling the loss.

4. Depression:

   Eventually, after a person has denied, raged and bargained they begin to realise the great loss they have suffered and this may result in depression. They need to receive acceptance, understanding and empathy, and be given space to freely express their feelings to help them through this period.

5. Acceptance:

   Eventually the loss is accepted and the person begins to adjust to the changes the loss has brought to their life. At first there is a feeling of numbness which becomes a very sad period. Although this sadness will be overcome and the person will continue with their life, at times in the future they will be reminded of their loss, resulting in sadness or anger once again. Before reaching acceptance, some people may move forward and backward through the above stages while others may only go through some of the stages.

THE NORMAL RESPONSE TO LOSS IS A SEQUENCE OF DENIAL, ANGER, BARGAINING, DEPRESSION AND ACCEPTANCE
52-40 CAN REACTIONS TO LOSS BE ABNORMAL?

Yes. Some people have an abnormal grieving (mourning) reaction. They may take too long or not be able to pass from one stage to another, or have an abnormally strong reaction in a particular stage. Thus a person may become stuck in denial and be unable to come to terms with the bad news, have excessive anger, which can damage their relationships with family and friends, or cause them to blame caregivers, or become pathologically depressed.

52-41 WHAT IS THE RESPONSIBILITY OF THE GENETIC COUNSELLOR IN THESE SITUATIONS?

The genetic counsellor needs to be aware that abnormal grieving reactions can develop, be able to recognise them as early as possible and refer the person for expert management.

PARENTS’ CHOICES WITH PRENATAL DIAGNOSIS

52-42 WHAT CHOICES DOES A WOMAN HAVE WITH A CONFIRMED PRENATAL DIAGNOSIS OF A BIRTH DEFECT?

Once a pregnant woman, preferably together with her partner, has received careful genetic counselling regarding her specific situation, she should consider the options available to her. It is particularly important that she is given detailed information about the severity of the disability and the mortality risk associated with the specific birth defect. The health care facilities available to manage an infant born with that particular birth defect must also be known. Only then, can she make a choice of:

1. Continuing with the pregnancy.
2. Having a termination of pregnancy.

52-43 WHAT FACTORS WILL AFFECT HER CHOICE?

1. The gestational age.
2. The severity of the defect.
3. Her and her partner’s feelings about termination.
4. The health care facilities ability to manage the infant if born alive.
5. The laws of the country with regard to the termination of pregnancy.

52-44 AT WHAT GESTATIONAL AGE IS TERMINATION OF PREGNANCY FOR FETAL ABNORMALITY LEGAL IN SOUTH AFRICA?

1. Any woman may request a termination during the first 12 weeks of pregnancy (measured from the first day of the last normal menstrual period).
2. From 13 to 20 weeks gestation a woman may be offered a termination if there is a “substantial risk that the fetus would suffer from a severe physical or mental abnormality”.
3. After 20 weeks gestation a woman may be offered a termination if the continued pregnancy would result in “a severe malformation of the fetus or pose a risk of injury to the fetus”

Therefore, termination is allowed up to 20 weeks gestation for a high risk of severe fetal abnormality, and beyond 20 weeks if the fetus is known to have a severe fetal abnormality. The definition of severe abnormality is not given in the Act.

IN SOUTH AFRICA A TERMINATION OF PREGNANCY IS ALLOWED BY LAW FOR A SEVERE FETAL ABNORMALITY

*** The Choice on termination of pregnancy act (Act 92) was passed in 1966.
52-45 WHERE ARE TERMINATIONS OF PREGNANCY PERFORMED?
In clinical or hospitals which are registered to perform surgical terminations.

52-46 WHAT SPECIFIC COUNSELLING IS NEEDED WHEN A WOMAN CHOOSES TO HAVE A TERMINATION OF PREGNANCY?
It is extremely important that the woman (and her partner) are well counselled before a termination of pregnancy. They need to appreciate all the implications. There is always an emotional price to pay. It is essential that the woman considers all the advantages and disadvantages before finally making her choice.

PARENTS MUST BE VERY WELL COUNSELLED BEFORE CONSIDERING A TERMINATION OF PREGNANCY

Women with a gestational age of 13 weeks or more need to be counselled and informed that they may have to stay in hospital for 2 to 4 days. They also need to know about the procedure. Women often believe incorrectly that a pregnancy can be terminated easily and quickly.

52.47 WHAT METHODS ARE USED TO TERMINATE A PREGNANCY?
The method depends on the gestational age at which the termination is performed:

1. Before 13 weeks gestational age, misoprostil (Cytotec) is given orally or inserted into the vagina. Two tablets (1 tablet = 200 µg) are given immediately and then another two given 6 hours later. This is done at home in the evening and the patient is seen again the next morning. Usually the cervix will be soft and partially dilate so that a manual vacuum aspiration can be performed following infiltration of local anaesthetic into the cervix. This procedure can be done as an outpatient procedure.

2. From 13 to 19 weeks gestational age, patients must be admitted in hospital. A termination of pregnancy is induced with misoprostil. One tablet (1 tablet = 200 µg) is given every 4 hours for a total of 4 doses. Often this may not be enough and this regimen has to be repeated following day. In some cases prostaglandin E2 (Prepidil gel) or prostaglandin F2 alpha may be required in addition. Once the fetus has delivered, an evacuation of the uterus is done. A manual vacuum aspiration could be used for women with a gestational age of 14 weeks or less as mentioned above. However, those women with a more advanced pregnancy may not abort completely and will require an evacuation in theatre under general or spinal anaesthetic using a large ovum forceps and large sharp curette.

52-48 WHAT FOLLOW UP IS NEEDED AFTER A TERMINATION OF PREGNANCY FOR A BIRTH DEFECT?
All women that have their pregnancies terminated for a severe birth defect must be followed up at 4 to 6 weeks to be counselled again about the reason for the termination and to ask them about their feelings.

Family planning is advisable in all cases following termination of pregnancy as they require time to resolve the emotional impact of the termination. Once they reach a stage of acceptance a decision regarding further pregnancies or a permanent form of contraception can be made.
52-49 WHAT ARE THE EMOTIONAL AND PHYSICAL RISKS OF A TERMINATION OF PREGNANCY FOR A BIRTH DEFECT?

Termination of pregnancy for an abnormal fetus has a profound emotional impact on a woman and her husband or partner. It is therefore important to reinforce the reason why she made the decision and what was wrong with the fetus. Ample time for questions must be allowed and the parents must also be asked about their feelings and how they are coping at home. These women often have feelings of:

1. Failure and having let their husband or partner and family down.
2. Guilt, because the abnormal fetus may have been the result of something they did or did not do. They also often feel guilty about their decision to terminate the pregnancy.

The physical risks are small, provided the medical management is done safely. However there are small risks of:

1. Excessive haemorrhage during the termination.
2. Perforation of the uterus during evacuation.
3. Infec tion (endometritis) following the evacuation.
5. A rupture of the uterus with more advanced gestational ages (22 to 25 weeks). In these more advanced pregnancies the dose of misoprostil must be reduced to 100 µg per dose.

CASE PROBLEMS

CASE 1.

A woman who is one month pregnant, and has a three year old child with a birth defect, visits her family doctor and asks if anything can be done to find out whether her fetus has the same birth defect. After taking a careful family history, the doctor draws a three-generation family tree.

1. How can birth defects be diagnosed during pregnancy?
   (i) Older women (35 years or older) are at an increased risk of having a fetus with birth defects, especially Down syndrome. They should be counselled and screened and, if necessary, offered prenatal diagnosis (amniocentesis).
   (ii) Ultrasound scanning can detect many birth defects.
   (iii) Blood tests can be used to screen for some defects such as neural tube defects.

2. What can be done before pregnancy to reduce the risk of child with birth defects?

The risk of having having a child with birth defects can sometimes be reduced with basic reproductive health approaches, such as family planning and peri-conceptional care.

3. What is peri-conceptional care?

This is the care of women before conception and during the first eight weeks of pregnancy, which may reduce the risk of birth defects.
4. **Give a few examples?**

(i) Improve the woman’s diet by food supplementation or fortification.
(ii) Avoid dangerous substances, such as alcohol.
(iii) Make sure that all women are immunised against rubella before they reach childbearing age.
(iv) Detect and correctly treat maternal illnesses such as diabetes and epilepsy.
(v) Make sure that any medication taken is safe for the fetus.

5. **What are supplementation and fortification?**

Essential substances, such as folic acid and iodine, can be added to food in the diet (fortification) or can be taken separately as a pill, tablet or capsule (supplementation). Folic acid and iodine are often provided as either fortification or supplementation.

6. **What is a three-generation family tree?**

This is a graphic representation (a drawn plan) of three generations of that family showing normal individuals and those who have a birth defect or are carriers of a birth defect.

7. **What is the value of a three-generation family tree?**

It helps to identify patterns of inheritance of a birth defect, e.g. dominant, recessive or X-linked. This makes it easier to predict whether a birth defect is likely to occur in a given pregnancy.

CASE 2.

Parents who plan a family are concerned about the possibility of having a child with birth defects. They speak to friends and say they have heard about medical genetic screening for birth defects but do not know what the term means.

1. **What is medical genetic screening?**

Medical genetic screening, or population screening, is a system that uses questions and tests in a community to identify individuals at increased risk of birth defects.

2. **What is the importance of identifying people at increased risk?**

They can be offered further tests to confirm whether or not they, or their fetus, have the birth defect or are likely to pass the problem on to their children.

3. **Do these people not already have signs of the clinical condition?**

No. This is why they need to be identified by a screening method.

4. **What is the importance of being identified as having a birth defect or possibly passing a genetic defect on to ones’ children?**

Prevention or treatment can be offered to these people. For example, they may decide not to have children if there is a high chance that their children may be affected by a serious genetic defect, such as cystic fibrosis. On the other hand, the infant could be offered treatment for a condition, such as haemophilia, before it presents with serious complications.

5. **When can screening be done to prevent birth defects?**

(i) Before conception (pre-conception screening or primary prevention).
(ii) During pregnancy (antenatal screening or secondary prevention).
(iii) After delivery (postnatal screening or tertiary prevention).
6. **Can you give an example of each?**

(i) Before conception – DNA carrier screening for single gene defects.
(ii) During pregnancy – Early ultrasound scanning for Down syndrome.
(iii) After delivery – blood screening for congenital hypothyroidism.

**CASE 3.**

A nurse wants to train as a genetic counsellor. She speaks to the tutor of a genetic counselling course to find out more about counselling. She also reads a book about caring for parents of children with birth defects.

1. **What is genetic counselling?**

It is a process of education, communication and support which helps people who are affected by a birth defect or are at risk of inheriting or passing on a birth defect to their children. It enables them to understand their problems, make appropriate decisions and come to terms with their situation.

2. **What are the main goals of genetic counselling?**

The main goals of a genetic counsellor are:

(i) Define the problem.
(ii) Informing and educating.
(iii) Allowing people to make their own decisions.
(iv) Supporting them.

Remember “DIAS”.

3. **Why is counselling more than simply giving good advice?**

During counselling, people are educated about their problems, receive options for managing the situation and are empowered to try and understand their problem and then make the best decision for themselves. They are helped to deal with their feelings and encouraged to make their own decisions according to their personal circumstances. The counsellor should accept their choices and support them in their decision.

4. **What essential skill does a genetic counsellor need?**

They should be able to communicate well with people. Active listening is particularly important.

5. **What is active listening?**

It is the ability to hear not only the words people say but also note their body language and emotional reactions. This helps to understand the meaning behind their words.

6. **What are common mistakes, which may prevent active listening?**

(i) Talking more than listening.
(ii) Interrupting and arguing.
(iii) Being judgmental.
(iv) Concentrating only on facts and not also feelings.
7. What are the expected normal responses to loss?

(i) Denial.
(ii) Anger.
(iii) Bargaining.
(iv) Depression.
(v) Acceptance.
OBJECTIVES

When you have completed this unit you should be able to:

1. Recognise an infant or child with Down syndrome.
2. Understand the causes of Down syndrome.
3. Explain the risk factors for Down syndrome.
4. List the clinical features and complications of Down syndrome.
5. Describe how Down syndrome can be diagnosed antenatally.
6. Plan the care of a child with Down syndrome.
7. Understand how the risk of having an infant with Down syndrome can be reduced.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way, nor may copies of the complete Programme be made, without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, however, parts of the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme are believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.

ISBN 0 7992 2254 2
53-1 WHAT IS DOWN SYNDROME?

Down syndrome is the name given to a characteristic pattern of clinical features and birth defects that includes a typical facial appearance, intellectual disability, hypotonia, congenital heart defects and growth retardation. These children can be recognised by their physical appearance. They all have a similar appearance.

### INDIVIDUALS WITH DOWN SYNDROME CAN BE RECOGNISED CLINICALLY

Down syndrome is the correct term for this condition although it is often incorrectly called Down's syndrome. The old terms “Mongol” and mongolism are not acceptable and are no longer used. Down syndrome is a typical example of a chromosomal disorder.

*** The syndrome was first described in 1866 by Dr Langdon Down in London. A syndrome is a collection of clinical features and birth defects that can be recognised as forming a consistent pattern.

53-2 HOW COMMON IS DOWN SYNDROME?

Down syndrome occurs in all communities and ethnic groups. In developing (low resourced) countries the birth prevalence (number of affected infants at birth) is 2 to 3 per 1000 live births. In industrialised (high income) countries, the birth prevalence is less than 1.5/1000 live births.

In South Africa the birth prevalence of Down syndrome is 2.1/1000 live births in the Limpopo Province (a poor rural area) and 1.8/1000 in Soweto (a more developed urban area).

The prevalence (number of affected infants and children per 1000 children in the community) falls rapidly in developing countries as many affected children die in infancy or early childhood.

In Limpopo Province the prevalence of Down syndrome in children aged two to nine years is only 0.74/1000, indicating that 65% of affected children have already died by two years of age.

### THE BIRTH PREVALENCE OF DOWN SYNDROME IN SOUTH AFRICA IS ABOUT 2 PER 1000 LIVE BIRTHS

53-3 WHY IS THE BIRTH PREVALENCE OF DOWN SYNDROME HIGHER IN DEVELOPING COUNTRIES?

The risk of a woman having an infant with Down syndrome increases as she gets older. It is especially high once she reaches 35 years. Advanced maternal age (AMA) is the term used to describe pregnant women of 35 years or older.

In developing countries, 11 to 14% of pregnant women are of advanced maternal age compared with only 5 to 9% in industrialised countries. The greater the percentage of women of advanced maternal age having infants, the higher will be the birth prevalence of infants with Down syndrome.

In industrialised countries, women are aware of their increased risk of having a child with Down syndrome. Therefore, most use family planning and choose not to fall pregnant over 35 years of age. This lowers the percentage of pregnant women of advanced maternal age and, therefore, reduces the birth prevalence of Down syndrome in these countries.

*** In China, because of the one child per family policy, women usually choose to have their child between 25 and 27 years of age. Pregnant women of advanced maternal age are rare. Therefore, the birth prevalence of Down syndrome in China is very low, less than 1/1000 live births.

PERINATAL EDUCATION PROGRAMME
THE RISK OF HAVING AN INFANT WITH DOWN SYNDROME INCREASES WITH ADVANCED MATERNAL AGE

Figure 53-1: The birth prevalence of Down syndrome and all chromosomal abnormalities in women of increasing age.

<table>
<thead>
<tr>
<th>Maternal Age in years</th>
<th>Birth prevalence of live born infants with Down syndrome</th>
<th>Birth prevalence of all live born infants with chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1/1000</td>
<td>1/450</td>
</tr>
<tr>
<td>20</td>
<td>1/1734</td>
<td>1/536</td>
</tr>
<tr>
<td>25</td>
<td>1/1250</td>
<td>1/476</td>
</tr>
<tr>
<td>30</td>
<td>1/965</td>
<td>1/385</td>
</tr>
<tr>
<td>35</td>
<td>1/386</td>
<td>1/192</td>
</tr>
<tr>
<td>36</td>
<td>1/300</td>
<td>1/156</td>
</tr>
<tr>
<td>37</td>
<td>1/234</td>
<td>1/127</td>
</tr>
<tr>
<td>38</td>
<td>1/182</td>
<td>1/102</td>
</tr>
<tr>
<td>38</td>
<td>1/141</td>
<td>1/83</td>
</tr>
<tr>
<td>40</td>
<td>1/110</td>
<td>1/66</td>
</tr>
<tr>
<td>41</td>
<td>1/86</td>
<td>1/53</td>
</tr>
<tr>
<td>42</td>
<td>1/66</td>
<td>1/42</td>
</tr>
<tr>
<td>43</td>
<td>1/53</td>
<td>1/33</td>
</tr>
<tr>
<td>44</td>
<td>1/40</td>
<td>1/26</td>
</tr>
<tr>
<td>45</td>
<td>1/31</td>
<td>1/21</td>
</tr>
<tr>
<td>46</td>
<td>1/24</td>
<td>1/16</td>
</tr>
<tr>
<td>47</td>
<td>1/19</td>
<td>1/13</td>
</tr>
<tr>
<td>48</td>
<td>1/15</td>
<td>1/10</td>
</tr>
<tr>
<td>49</td>
<td>1/11</td>
<td>1/8</td>
</tr>
</tbody>
</table>

Note that the risk of Down syndrome increases almost three fold between 30 and 35 years of age from 1/965 (approximately 1/1000) to 1/386 (approximately 2.6/1000).

53-4 ARE MOST INFANTS WITH DOWN SYNDROME BORN TO OLDER WOMEN?

Yes. In South Africa, and most other developing countries where a higher percentage of pregnant women are of advanced maternal age, most infants with Down syndrome are born to older mothers. In South Africa more than half (above 50%) of infants with Down syndrome infants are born to mother aged 35 years or older.

In industrialised countries, where women use contraception and a lower percentage of mothers are of advanced maternal age, most infants with Down syndrome (above 60%) are born to mothers under 35 years of age.

53-5 IS DOWN SYNDROME WELL KNOWN IN ALL COMMUNITIES?

In industrialised countries, Down syndrome is well researched and publicised so that most members of the community know about the condition. In contrast, the condition is not well known in many developing communities, who may not even have a local name for the condition. The lack of awareness of Down syndrome in many rural communities in South Africa results in many affected children being undiagnosed. This situation is improving with education to inform health care workers and the community about Down syndrome.
In the early 1990s in Gauteng Province only 3% of mothers of infants with Down syndrome were aware of the condition before the birth of their infant. By 1997, due to education of the community and medical and nursing staff, 47% of mothers presenting for AMA counselling knew of Down syndrome.

53-6 WHAT IS THE CAUSE OF DOWN SYNDROME?

Down syndrome is the commonest chromosomal disorder in live born infants. It is caused by extra material from chromosome 21 being present in the body’s cells. Individuals with Down syndrome usually have three, instead of the normal two, chromosomes 21 in all body cells. This is called trisomy 21 (tri=3). Because of the extra chromosome 21, each cell now has a total of 47 chromosomes instead of the normal 46. An extra chromosome 21 (non-disjunction resulting in trisomy 21) is the cause of Down syndrome in more than 95% of affected children. The risk of recurrence is low.

DOWN SYNDROME IS CAUSED BY THE PRESENCE OF EXTRA CHROMOSOME 21 MATERIAL IN THE CELLS OF THE BODY

Figure 53-2: The appearance of the chromosomes in trisomy 21 (karyotype). Note that there are three instead of the normal two chromosomes 21.
About 3% of infants with Down syndrome do not have a whole extra chromosome 21 but an extra piece of a chromosome 21 is added (translocated) onto another chromosome. The total number of chromosomes is therefore normal at 46 (but one of the chromosomes looks longer than usual as it has an extra piece of a chromosome 21). This is called translocation Down syndrome. In the other 2% of infants with Down syndrome, only some of their body cells have an extra chromosome 21. This is known as mosaicism.

**DOWN SYNDROME IS ALMOST ALWAYS DUE TO TRISOMY CAUSED BY NON-DISJUNCTION**

The appearance of children with Down syndrome is the same whether the extra chromosome 21 material is due to trisomy, translocation or mosaicism.

*** The features of Down syndrome are caused by genes on a relatively small piece of the long arm of chromosome 21. The translocated piece is usually added to chromosomes 13, 14, 21 or 22. This may be a new defect or be inherited from a parent with a balanced translocation. In the latter, there is an increased risk of recurrence.

Trisomy, mosaicism and translocation are discussed further in unit 51 of the Perinatal Education Programme.

**53-7 HOW DOES TRISOMY 21 OCCUR?**

Trisomy 21 (having an extra chromosome 21) is caused by non-disjunction. This is an imbalance in the sharing of the 46 chromosomes in the cells which divide into two in order to form the ova (eggs) before fertilization. In this division, each ovum (egg) should get 23 chromosomes. However, in non-disjunction this division is incorrect. The paired chromosomes 21 do not separate, as they should. Instead, one ovum gets two chromosomes 21, while the other ovum gets none. In trisomy 21, the ovum with two copies of chromosome 21 (instead of one) is fertilized by a normal sperm with one copy of chromosome 21. As a result, the zygote (the fertilised cell from which the fetus will develop) now has three copies of chromosome 21 (instead of two) with a total of 47 chromosomes.

Figure 53-2: Non disjunction to give trisomy 21.
*** While Down syndrome usually occurs because of non-disjunction in the ovum of the mother (80%), in 20% of people with Down syndrome the non-disjunction takes place in the father, and it is the sperm that has the extra chromosome 21.

53-8 How can one recognise a person with Down syndrome?

Infants, children and adults with Down syndrome, throughout the world, have a similar appearance. They have clinical features which can be recognised. However, the diagnosis of Down syndrome is frequently missed in infants in South Africa. To prevent this, the clinical diagnosis of Down syndrome must be based on a complete history and physical examination, and not just the facial appearance. The clinical diagnosis should be confirmed by a chromosome analysis, done on a blood sample.

*** In South Africa, research shows that only 16% of newborn infants with Down syndrome are diagnosed by health care workers in the hospital or clinic after delivery. Less than 50% of infants with Down syndrome are diagnosed before 6 months of age, even though they have attended clinics for their immunisations.

53-9 What are the main recognisable features of Down syndrome?

The main clinical signs of Down syndrome are:

1. Hypotonia (floppy infant).
2. A typical facial appearance.
3. Poor feeding.
4. Abnormalities of the hands and feet.
5. Poor Moro reflex.
7. Congenital heart defects.

53-10 What are the typical facial appearances of a person with Down syndrome?

There are a number of abnormalities seen in the face, head and neck of a person with Down syndrome.

1. Face:
   - A small, round, flat face.
   - Upward slanting eyes with epicanthic folds (prominent skin folds at the inner corner of the eyelids).
   - A flat nasal bridge.
   - Relatively big tongue and small, open mouth. Therefore, the tongue often protrudes (sticks out of the mouth).

2. Head:
   - The head is round with a flat occiput (back of the head). This is called brachycephaly.
   - The head circumference is often smaller than normal.
   - The ears are small and may be malformed and low set.

3. Neck:
   - The neck is short.
   - Skin over the back of the neck is loose, forming folds.
Photographs showing the typical features of Down syndrome are shown at the end of this unit.

53-11 WHAT ARE THE TYPICAL FEATURES OF THE HANDS OF A PERSON WITH DOWN SYNDROME?

Infants, children and adults with Down syndrome all have hands which look alike and can easily be recognised. The typical hand appearance includes:

1. Short, broad hands with short stubby fingers (brachydactyly).
2. Most have a single palmar crease on one or both hands.
3. They often have short, incurved small fingers (clinodactyly) and may only have a single crease on their little finger.

53-12 WHAT ARE THE TYPICAL FEATURES OF THE FEET OF A PERSON WITH DOWN SYNDROME?

Infants, children and adults with Down syndrome also have feet that look alike. The typical features are:

1. They are short and broad, similar to the hands.
2. A wide gap between the large and second toe is common (sandal gap).
3. A crease extending from the sandal gap towards the heel is common. This may not be obvious in children who do not wear shoes.

53-13 WHAT ARE THE SIGNS OF HYPOTONIA IN AN INFANT WITH DOWN SYNDROME?

Infants with Down syndrome are floppy (hypotonic) and have a poor Moro reflex. Obvious floppiness (hypotonia) is most marked during the first months of life. There is head lag and usually an incomplete Moro reflex. Hypotonia is the most consistent sign in Down syndrome. When handled, infants feel like a rag doll. Mothers often complain when their infants reach four months of age and still do not have head or neck control. As children with Down syndrome grow older the hypotonia become less obvious.

53-14 WHY DO INFANTS WITH DOWN SYNDROME FEED POORLY?

Infants with Down syndrome often have feeding difficulties during the first weeks of life. They feed slowly with a poor suck and have difficulty swallowing due to the relatively big tongue. Feeds may have to be given by tube or cup at first before they can breastfeed adequately. Their hypotonia and frequent blocked nose contribute to the feeding problems. However, over the weeks their feeding improves. Heart failure, caused by congenital heart defects, may also cause poor feeding, and needs to be treated.

53-15 ARE ALL PEOPLE WITH DOWN SYNDROME INTELLECTUALLY DISABLED?

Down syndrome is the commonest genetic cause of developmental delay and intellectual disability. The milestones of infants and children with Down syndrome are slow, co-ordination is poor, and language and social development is delayed. They are all intellectually disabled to a greater or lesser degree. However, the degree of intellectual disability varies widely. With early and appropriate encouragement and stimulation, the level of intellectual disability can be improved. These children can then be mainstreamed into normal schools, although their progress will be slow and they will need special attention. This is the current educational policy in South Africa. As adults, they work well and many find work in the open labour market or in sheltered employment. South Africa’s new labour laws promote the employment of people with disability.

PERINATAL EDUCATION PROGRAMME
Unfortunately, the degree of impaired learning disability has been exaggerated in the past when little effort was made to encourage these children to reach their developmental potential. With late or little stimulation, intellectual disability is often severe, further disadvantaging them and hindering their integration into society.

*** The term intellectual disability is preferred to mental retardation.

53-16 WHAT IS THE PATTERN OF GROWTH IN INFANTS WITH DOWN SYNDROME?

Most South African newborns with Down syndrome are born at term (37 to 42 weeks) and have an average birth weight of 2700g, which is less than normal, and a sign that their fetal growth is slower than usual. After birth, infants and children with Down syndrome continue to grow slowly and remain shorter than normal (stunted). Weight gain is slow in the first months and years but many children with Down syndrome later become obese. Obesity remains a problem in adolescence and adulthood.

*** Older children with Down syndrome in rural areas tend not to be obese. This is because the supply of food is limited and they get adequate exercise as they have to share the family and household chores.

53-17 WHO USUALLY MAKES THE CLINICAL DIAGNOSIS OF DOWN SYNDROME?

The diagnosis should be made by the nurses or doctors caring for the infant after delivery. However, the clinical features can be difficult to recognise in the first few days of life. Some mothers are first to notice that their newborn infants do not appear normal or have problems. If the mother is concerned, the infant must be examined carefully.

The way to identify infants and children with Down syndrome is to make sure you know and can recognise their clinical features. Always look for Down syndrome, especially in infants and children of older mothers and infants who are floppy. Take a full history and complete a general examination, being certain to look for hypotonia, a poor Moro reflex, and abnormalities of the hands and feet. Confirm the diagnosis with a chromosome test done on a blood sample.

53-18 WHEN SHOULD PARENTS BE TOLD THE DIAGNOSIS OF DOWN SYNDROME?

It is important to tell the parents the diagnosis as soon as possible. The manner in which they are told and counselled has a major effect on the way they accept the diagnosis. With careful examination, most infants with Down syndrome should be diagnosed at birth or shortly thereafter.

THE COMPLICATIONS OF DOWN SYNDROME

53-19 WHAT ARE THE MAJOR COMPLICATIONS OF DOWN SYNDROME IN CHILDREN?

1. **Congenital heart defects**: These are a frequent cause of early death. Congenital heart defects often cause heart failure which can result in recurrent pneumonia.
2. **Recurrent infections**: Children with Down syndrome have poor functioning of the immune system, and this causes recurrent infection, especially of the upper respiratory tract and lungs (pneumonia). This is worsened by a poor ability to cough due to the hypotonia. Pneumonia is a common cause of death in children with Down syndrome, especially in the first few years of life.
3. **Visual problems**: Squint, nystagmus (horizontal or vertical jerky movements of the eyes) and short or long sightedness are common. Cataracts are less common. Many children with Down syndrome need to wear glasses.
4. **Hearing problems:** This is most often caused by repeated middle ear infections with fluid behind the ear drum (in the middle ear).

5. **Hypothyroidism:** This can occur at any age in a person with Down syndrome and is difficult to diagnose. Routine testing at birth, six months of age and then yearly thereafter should be done to screen for hypothyroidism.

*** Myeloid leukaemia and an unstable cervical joint in the neck are rare but important complications of Down syndrome. They often also have early onset Alzheimer’s disease as young adults (as early as 25 to 30 years).

53-20 WHAT BIRTH DEFECTS ARE IMPORTANT COMPLICATIONS OF DOWN SYNDROME IN THE NEWBORN INFANT?

1. **Congenital heart defects:** 40-45% of infants and children with Down syndrome have congenital heart defects. They may present with features of heart failure, failure to thrive or cyanosis (blue). Some are detected when a heart murmur is heard during routine clinical examination.

2. **Duodenal atresia:** These infants have an obstruction in the duodenum (between the outlet of the stomach and the start of the small intestine). They vomit their feeds in the first few days of life and the vomitus is often bile stained. The diagnosis can be confirmed on an abdominal X-ray, by the presence of what is called a “double bubble” (the dilated stomach and upper duodenum). They must be urgently transferred for corrective surgery.

*** Both duodenal atresia and some congenital heart defects can be diagnosed by antenatal ultrasound examination.

53-21 WHICH ARE THE COMMONEST CONGENITAL HEART DEFECTS IN CHILDREN AND INFANTS WITH DOWN SYNDROME?

Almost a half of all infants with Down syndrome have some form of heart defects. The congenital heart defects that occur include:

1. **Endocardial cushion defect:** (a hole between the atria and ventricles of the heart). 20% of congenital heart defects in infants and children with Down syndrome are endocardial cushion defects.

2. **Ventricular septal defect:** (VSD - a hole in the wall which separates the two ventricles, the lower two chambers of the heart). This may be small, which causes little or no clinical problems and closes without treatment in the first year of life. However, it may be large, causing severe problems in the first weeks of life, including heart failure, repeated episodes of pneumonia and failure to thrive. In these children, medical and possibly surgical treatment is indicated.

3. **Atrial septal defect:** (ASD – a hole in the wall between the atria, the upper two chambers of the heart).

4. **Tetralogy of Fallot:** This is a complex heart defect in which the child is cyanosed (blue).

Congenital heart defects are the commonest cause of death in infants and children with Down syndrome. Therefore, all newborn infants with Down syndrome must be carefully examined for signs of congenital heart defects.

### CONGENITAL HEART DEFECTS ARE THE COMMONEST CAUSE OF DEATH IN CHILDREN WITH DOWN SYNDROME

*** Endocardial cushion, ventricular septal and atrial septal defects result in excessive blood flow through the lungs. These congested, oedematous lungs are very susceptible to infections, which are often the cause of death if not correctly treated.

PERINATAL EDUCATION PROGRAMME
WHAT IS THE LIFE EXPECTANCY OF CHILDREN WITH DOWN SYNDROME?

The life expectancy varies widely between different countries. In developing countries, most children with Down syndrome die during infancy and early childhood from infections and congenital heart defects. In South Africa 65% of infants and young children with Down syndrome die before the age of 2 years. In contrast, most children with Down syndrome in industrialised countries can be expected to survive into adulthood, with many living between 50 to 60 years of age.

Young women with Down syndrome are usually fertile. Contraception for them is very important. They have a 50% chance of having an infant with Down syndrome.

CARING FOR CHILDREN WITH DOWN SYNDROME

WHAT CARE IS AVAILABLE FOR INFANTS AND CHILDREN WITH DOWN SYNDROME?

Infants and children with Down syndrome, as with all people with congenital disability, should be offered the “best possible care” available for their problems and special needs. This care includes:

1. Diagnosis:

For infants and children with Down syndrome, as with all persons with birth defects, it is important to make and confirm a diagnosis as early as possible. This allows for early genetic counselling to inform parents about the disorder, its cause and available treatment. It also helps families come to terms with the condition, and accept and bond with their child. This will encourage the parents to begin early treatment and stimulation programmes, to enable the child to reach his or her best long-term potential for health, development and intellectual ability.

2. Medical treatment:

Infants and children with Down syndrome have many problems that require medical treatment, which can be offered in primary health care facilities. Heart failure from congenital heart defects can be diagnosed and treated with anti-failure drugs (digoxin, diuretics and potassium chloride). The child may need referral for special investigations to confirm the cardiac diagnosis and to plan surgery if necessary and available.

Recurrent infections should be treated early and vigorously with antibiotics. Iron and multivitamin supplements should also be prescribed.

Infants and children with Down syndrome should be tested for hypothyroidism, and treated if necessary.

Children with Down syndrome who have congenital heart defects need protection against bacterial endocarditis (infection of the heart valves) after dental care or surgery. They must receive prophylactic antibiotics before and after these procedures.

All infants and children with Down syndrome should receive routine immunisations.

3. Surgical treatment:

Surgical repair for some congenital heart defects may be available in paediatric cardiac units.

Infants and children with Down syndrome who have visual problems, including squint, nystagmus, cataracts and poor vision, should be referred for an ophthalmological (eye) assessment.
Infants and children with Down syndrome who have other birth defects like duodenal atresia will need surgical correction of these problems. Boys with Down syndrome often have undescended testes, which may need surgery if undescended after age 2 years.

4. Neurodevelopmental therapy and community based rehabilitation:

This is a very important part of caring for children with Down syndrome.

5. Genetic counselling and psychosocial support.

53-24 HOW CAN INFANTS AND CHILDREN WITH DOWN SYNDROME BE HELPED TO REACH THEIR FULL DEVELOPMENTAL AND INTELLECTUAL POTENTIAL?

Infants and children with Down syndrome develop slowly and all are intellectually disabled to some degree. It has been proved that infants and children with Down syndrome who receive good early neurodevelopment therapy, love and stimulation from their parents at home, have a better intellectual outcome (IQ) than those put in institutions or neglected. The earlier they are referred for intervention and stimulation, the better the results.

Neurodevelopmental therapy includes the following:

1. **Physiotherapy** is very useful for infants who are floppy and have slow motor milestones. It helps these infants and young children to achieve their motor milestones faster. For the best result, referral as young as possible is recommended.
2. **Hearing assessment (audiology) and speech therapy** are important for infants and children with Down syndrome as they have delayed speech development. This is worsened by recurrent ear infections which may cause hearing loss. If deafness is suspected, a hearing assessment should be done. Speech therapy helps the development of better speech. Again, early referral gives the best results.
3. **Occupational therapy** can improve fine motor co-ordination as well as personal and social development. Early assessment and therapy give the best results.

All these forms of neurodevelopmental therapy are available in major centres. However, in both rural and urban areas regions with fewer resources, hospitals may only have a physiotherapist and/or an occupational therapist. A few may also have a community based rehabilitation programme.

In South Africa, rehabilitation for infants and children with disabilities, including Down syndrome, can be assisted by the use of a locally produced stimulation programme called START (Strive Towards Achieving Results Together). This was designed to use cheap, locally available materials. This programme is of great benefit to infants and children with Down syndrome. Every effort must be made to keep the child with Down syndrome in the home with their families so that they can be given the opportunity of fulfilling their emotional, health and educational needs.

*** Information on START can be obtained from, Sunshine Centre, P O Box 411567, Craighall, 2024. Telephone 011 642 2005.

*** The World Health Organisation has recognised that, given the different circumstances of each country, the levels of care available for people with congenital disability may differ. However, they consider that at all times the “best possible patient care” in the circumstances must be offered. The rights of all people with disability are protected in the Constitution of South Africa.
53-25 CAN DOWN SYNDROME BE PREVENTED?

Yes. There are two approaches for the prevention of Down syndrome. These are:

1. Primary prevention by trying to stop infants with Down syndrome being conceived. This pre-conception approach is the preferred method of prevention. It is based on the knowledge that the risk of having an infant with Down syndrome is greatest in women of 35 years of age or more. If women are made aware of Down syndrome and have access to family planning and contraception, they have the option of completing their families before the age of 35 years. In South Africa, up to 50% of Down syndrome pregnancies could be prevented in this manner.


DOWN SYNDROME CAN BE PREVENTED BEFORE CONCEPTION BY COMMUNITY EDUCATION AND FAMILY PLANNING, AND IN THE ANTENATAL PERIOD BY PRENATAL DIAGNOSIS AND GENETIC COUNSELLING

*** In Europe between 1950 and 1970, when women increasingly used family planning, the birth prevalence of Down syndrome dropped from 2.5 to 1.5 per 1000 live births. This was in a period when prenatal diagnosis of Down syndrome was not yet available.

SCREENING FOR DOWN SYNDROME

53-26 HOW CAN DOWN SYNDROME BE SCREENED FOR DURING PREGNANCY?

There are a number of methods which can identify pregnant women at high risk of having an infant with Down syndrome:

1. By identifying all pregnant women of advanced maternal age:

   This should be done at the first antenatal visit or, preferably, when pregnancy is first confirmed. Women aged 35 years or more should be offered genetic counselling, regarding their increased risk for an infant with Down syndrome, and the possibility of prenatal diagnosis, early in pregnancy. Identifying women of advanced maternal age is currently the only form of screening test for Down syndrome that can be offered to all women in South Africa. Unfortunately it is still not being done in many parts of the country.

2. Ultrasound examination of the fetus:

   This is best performed at 12 weeks of gestation (between 11 and 13 weeks). The thickness of the skin over the back of the fetal neck is measured. The skin thickness is usually increased with Down syndrome. As the ultrasonographer needs special training and expensive equipment, ultrasound screening is only available to a limited number of women in South Africa. Ultrasound screening is useful but will not detect all cases of Down syndrome. About 70% of fetuses with Down syndrome can be detected by ultrasound examination. Eleven to 13 weeks is also the best time to accurately determine gestational age by ultrasound examination. Other birth defects associated with Down syndrome may also be detected.

   *** Increased thickness of the skin over the back of the neck is due to a collection of fluid (increased nuchal translucency). This is strongly associated with a number of chromosomal abnormalities, especially Down syndrome. It is best to screen for nuchal translucency between 11 and 13 weeks gestation.
3. **Maternal serum screening during early pregnancy (the triple test):**

This is best done at 16 weeks (between 15 and 18 weeks) and requires that the gestational age is accurately known and confirmed by ultrasound examination. In the triple test, the concentrations of three biochemical compounds are measured in the mother’s blood. The test results, together with the gestational age and the maternal age, are entered into a computer programme to generate a risk for the fetus having Down syndrome.

*** If the fetus has Down syndrome, the concentration of maternal serum alpha fetoprotein (AFP) and unconjugated oestriol (uE3) tend to be decreased and human chorionic gonadotropin (hCG) increased.

4. **Maternal serum and ultrasound screening combined:**

Together these tests can detect up to 85% of fetuses affected with Down syndrome.

*** Recent research suggests that the triple test plus serum inhibin A concentration at 16 weeks, together with ultrasonography plus pregnancy associated protein A (PAPP A) concentration at 12 weeks gestation, will add even further to the accuracy of diagnosing Down syndrome giving an accuracy of 95% with only 5% false positives.

53-27 **WHAT SHOULD BE DONE IF ANTENATAL SCREENING INDICATES A HIGH RISK OF DOWN SYNDROME?**

If there is an increased risk for Down syndrome on genetic screening (advanced maternal age, ultrasound, maternal serum screening or a combinations of these), then the mother (preferably with her partner) should be counselled and offered prenatal diagnosis with amniocentesis at 16 weeks to confirm the possible diagnosis of Down syndrome.

53-28 **WHAT INVESTIGATIONS CAN CONFIRM OR EXCLUDE THE DIAGNOSIS OF DOWN SYNDROME?**

1. Chromosomal analysis can be used to confirm the diagnosis of Down syndrome in the fetus (prenatal diagnosis on amniotic fluid) or infant, child or adult (postnatal diagnosis on blood). The test takes 14 to 21 days before a result is obtained.
2. If the diagnosis of Down syndrome needs to be confirmed faster than 14 to 21 days, the diagnosis can be made in 48 to 72 hours using FISH (Fluorescent In-situ Hybridisation) or PCR-aneuploidy tests. These tests can detect an abnormal number of chromosomes 13, 18, 21, X and Y. However, they do not give as complete a result as chromosome analysis.

**GENETIC COUNSELLING FOR DOWN SYNDROME**

53-29 **WHAT GENETIC COUNSELLING IS NEEDED BY PARENTS WHO HAVE A CHILD WITH DOWN SYNDROME?**

Genetic counselling is a very important part of the care of people with Down syndrome and their family, especially the parents and siblings. The parents need to be educated and informed about:

1. The diagnosis.
2. The cause of Down syndrome. They need to know that Down syndrome is a genetic disorder, caused in 95% of cases, by an extra chromosome 21 (trisomy 21). The risk of this happening is greater in women of 35 years or more.
3. The clinical features, complications and prognosis of Down syndrome. Also what treatment that is available.
4. The increased risk for parents of a child with Down syndrome having another child with Down syndrome in future pregnancies. They need to know their options for reducing this risk by genetic screening and for preventing the birth of another affected child.
The parents, family and child with Down syndrome need to be offered ongoing psychosocial support, as with all individuals who have a congenital disability. They suffer lifelong problems that require lifelong care. The burden of the disorder and the care is experienced not only by the affected person, but also the family, especially parents, brothers and sisters.

53-30 WHERE CAN PARENTS, WHO HAVE A CHILD WITH DOWN SYNDROME, GET SUPPORT?

Support, help and reassurance may be obtained from:

1. Doctors, nurses (especially genetic-trained nursing staff), genetic counsellors and neurodevelopmental therapists.
2. Teachers in special schools for the intellectually disabled.
4. The Down Syndrome Association and other support groups play an important role in South Africa in helping persons and their families with Down syndrome. They are involved in educating the public, as well as medical and para-medical professions. They also play a major advocacy role for people with intellectual disability, including Down syndrome.

Contact details: Down Syndrome Association, P O Box 12962, Hatfield, Pretoria, 0028. Telephone/ Fax: 012 15941. E mail address: dssaoffice@icon.co.za Website: www.downsyndrome.org.za

Addendum C lists the addresses and contact details of the regional offices of the Down syndrome Association in South Africa.

Genetic counselling is fully discussed in unit 52 of the Perinatal Education Programme.

53-31 WHAT IS THE RISK OF A WOMAN, WITH ONE CHILD WITH DOWN SYNDROME, HAVING ANOTHER CHILD WITH DOWN SYNDROME?

This depends on the chromosomal diagnosis of the first child with Down syndrome, i.e. whether the child has trisomy 21, a translocation or mosaicism.

The risk for a woman less than 35 years old with an infant or child with trisomy 21 having an affected infant in future pregnancies is 1 in 100 (1%). If the woman is 35 or more years old, the risk is related to her age and is given as slightly higher than her age-related risk. In future pregnancies she should be offered amniocentesis.

If the child has a translocation involving an extra piece of chromosome 21, then the risk can vary greatly and be very high (100% recurrence risk in some cases), depending on the type of translocation. Therefore, a chromosome analysis for both parents needs to be known to be able to counsel them correctly. A counsellor with proper training and experience should do the counselling.

The risk for recurrence of mosaic Down syndrome is 1%.
53-32 WHAT CHOICES DOES A PREGNANT WOMAN HAVE IF SHE HAS AN INCREASED RISK FOR AN INFANT WITH DOWN SYNDROME?

If a pregnant woman is at increased risk for having a child with Down syndrome, she and her partner should receive genetic counselling. This counselling should fully inform them of what the risks are and the choices available to them. These include:

1. To have prenatal diagnosis. This will require an amniocentesis to be done to get fetal cells on which to perform chromosomal analysis, FISH or PCR-aneuploidy. Amniocentesis is offered between 16 and 21 weeks. Because this involves inserting a thin needle through the abdominal wall into the uterus, there is a risk that the procedure can cause complications, including a spontaneous miscarriage, vaginal bleeding or leaking amniotic fluid. This risk is about 1 in 140 (0.7%) with an experienced ultrasonographer. The woman should be informed of this before deciding whether she wants prenatal diagnosis.

2. She can continue the pregnancy without prenatal diagnosis, but knowing and understanding the risks for having an infant with Down syndrome.

53-33 WHAT CHOICES DOES A WOMAN HAVE WHEN A CONFIRMED PRENATAL DIAGNOSIS OF DOWN SYNDROME HAS BEEN MADE?

If a prenatal diagnosis of Down syndrome is confirmed, the woman, preferably with her partner, should urgently receive genetic counselling regarding the diagnosis and their choices.

For women at increased risk or with a prenatal diagnosis of Down syndrome, the choice of which options to take is theirs alone. Their medical care givers must respect this choice. They must also know that no matter what their choice, this will not influence their future routine care.

WITH GENETIC SCREENING AND PRENATAL DIAGNOSIS PEOPLE ARE ENTITLED TO GENETIC COUNSELLING AND ALWAYS HAVE THE RIGHT OF CHOICE

CASE STUDIES

CASE 1.

A 37 year old mother of two normal children asks whether she would be at increased risk of having an infant with Down syndrome if she planned another child. She wants to know how common Down syndrome is in South Africa and whether most infants with Down syndrome are born to older women.

1. **Is this woman at an increased risk of Down syndrome?**

   Yes. Because she is older than 35 years. At 37 years, her calculated risk is 1: 234 on the risk table. This is higher than a risk of 1:1250 for a woman who is 25 years old. Therefore, the risk is at least five times greater at 37 than at 25 years.

2. **What is the birth prevalence of Down syndrome in South Africa?**

   The birth prevalence of Down syndrome in South Africa is about 2 per 1000 live births.

3. **Why is the prevalence lower than the birth prevalence of Down syndrome in South Africa?**

   The prevalence (number of children with Down syndrome per 1000 children in the community) is lower than the birth prevalence because so many infants with Down syndrome die in the first few years of life. In rural areas of South Africa, the prevalence may be one third the birth prevalence, indicating that two thirds of these children die during infancy and early childhood.

PERINATAL EDUCATION PROGRAMME
4. Why is the birth prevalence of Down syndrome lower in industrialised than in developing countries?

Because the community is better informed about the risk of Down syndrome in pregnancy in older women. They, therefore, use family planning and have their infants before the age of 35 years. Genetic counselling and prenatal diagnosis is also more available in industrialized countries.

5. Are most infants with Down syndrome born to older women?

Yes, in developing countries such as South Africa. However, in industrialised countries, such as the USA and Europe, most infants with Down syndrome are born to younger women as the number of infants born to women over 35 years is small.

6. Why is Down syndrome often not recognised at birth in South Africa?

Because both the general community and health care workers are not informed about the condition and the typical clinical features. This is improving through education. It is important that the diagnosis is made and the parents be told he diagnosis and counselled as soon as possible.

CASE 2.

A midwife notices that a newborn infant does not appear normal. The mother says the infant does not look like her other five children. The infant has a small, flat face with upward slanting eyes, a flat nasal bridge and keeps sticking her tongue out. She is also very floppy and feeds poorly.

1. Does this infant have the typical facial appearances of Down syndrome?

Yes. She may also have a flat occiput, small ears and a lot of loose skin over the back of her neck. Some infants with Down syndrome do not have all the typical features.

2. What should the midwife look for if she examines the infant’s hands and feet?

Both hands and feet are short and broad. The hands may have a single palmar crease, and often a short little finger with a single finger crease. There is often a wide gap (sandal gap) between he first and second toe.

3. Are infants with Down syndrome often floppy with poor feeding?

Yes. They are all hypotonic (floppy) with a poor Moro reflex. As they grow older the hypotonia improves. Poor feeding in the first weeks of life is common in infants with Down syndrome. This is partly due to the relatively large tongue. Some are unable to breastfeed at first and may need to be fed expressed breast milk by cup.

4. What is the pattern of growth in infants with Down syndrome?

Most infants with Down syndrome are born at term but have a lower birth weight, length and head circumference than usual. They continue to grow slowly after birth. As adults they are short but may become obese.

5. What is the life expectancy in children with Down syndrome in an industrialised country?

Most can be expected to survive to between 50 and 60 years. However, in a developing country many die in childhood from infections and congenital heart defects. Therefore, the life expectancy varies widely between different countries.

PERINATAL EDUCATION PROGRAMME
CASE 3.

A three month old infant is brought to a local clinic where the diagnosis of Down syndrome had been made at birth. The mother says that the child gets very short of breath and becomes cyanosed (blue) with feeds. She wants to know whether her child will be able to attend a normal school.

1. **What is the probable complication in this child with Down syndrome?**

   It may have a congenital heart defect or pneumonia. Almost 50% of infants with Down syndrome have a congenital heart defect. Severe and recurrent infections, especially chest infections, are common. Congenital heart defects, such as a ventricular septal defect, often result in pneumonia.

2. **What other congenital malformation may presents in the first days of life?**

   Duodenal atresia. This is an obstruction in the duodenum which presents with repeated vomiting in the first few days of life. The vomitus is often bile stained. They need urgent referral to hospital for confirmation of the diagnosis and surgery.

3. **Do children with Down syndrome have normal intelligence?**

   No. They all have developmental delay and some degree of intellectual disability? They often also have visual and hearing problems which interfere with their speech development.

4. **Can they attend a normal school?**

   If possible they should attend a normal school. However they will need special help.

5. **How can children with Down syndrome be helped to reach their full developmental and intellectual potential?**

   They should receive love and early stimulation at home. Neurodevelopmental therapy, which is available at most major centres, will help them reach their developmental milestones sooner and have a better intellectual outcome (IQ). Community based rehabilitation programmes should be available for children with Down syndrome in smaller towns and rural areas. Every effort must be made to meet their emotional, health and educational needs.

CASE 4.

A primigravid woman with a 12 week pregnancy attends her first antenatal clinic. After receiving the routine antenatal care she has an ultrasound examination. She is asked to return the next day for further tests.

1. **Is an ultrasound examination a reliable method of screening for Down syndrome?**

   Ultrasound examination in early pregnancy is a very useful method of screening for Down syndrome. Between 11 and 13 weeks of pregnancy, many fetuses with Down syndrome can be detected (about 70%). Other birth defects may also be diagnosed.

2. **What other tests may be helpful to screen for Down syndrome?**

   A maternal serum test (triple test), done between 15 and 18 weeks, is very useful. Together with maternal age and an ultrasound examination, these screening tests will identify up to 85% of fetuses with Down syndrome.
3. **What should be done if the screening tests indicate a high risk for Down syndrome?**

After counseling, the woman should be offered an amniocentesis at 16 to 21 weeks gestation to obtain some fetal cells. Chromosomal analysis will confirm or exclude the diagnosis of Down syndrome. FISH and PCR-aneuploidy tests can also be used to identify trisomy.

4. **What should be done if the tests confirm Down syndrome?**

The woman, preferably with her partner, should be urgently referred for further genetic counselling. The diagnosis and implications of Down syndrome will be discussed. The woman will have to consider the choices of further management and decide on her option. The final decision rests with the couple, who must be assured that their choice will not influence their future routine care.
PHOTOGRAPHS OF CHILDREN WITH DOWN SYNDROME

Pictures 53–A: The typical facial appearance of children with Down syndrome, showing the round face, flat nasal bridge, epicanthic folds and low set ears.

Pictures 53-B: The typical hands of children with Down syndrome showing the single transverse palmar crease. The second picture shows clinodactyly and a single crease on the short fifth finger.

Picture 53-C: The typical foot of a child with Down syndrome showing the sandal gap between the big and second toe.
OBJECTIVES

When you have completed this unit you should be able to:

1. Define a single gene disorder.
2. Describe Waardenburg syndrome, oculocutaneous albinism, and haemophilia.
3. Explain how these conditions are inherited.
4. Recognise the clinical features of a person with any of these conditions.
5. List the clinical complications of these conditions.
6. Explain if and how these conditions can be diagnosed antenatally.
7. Plan the care of a person with these conditions.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way, nor may copies of the complete Programme be made, without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, however, parts of the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme are believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.
54.1 WHAT IS A SINGLE GENE DISORDER?

This is a clinical disorder caused by a defect in a single gene. The number of chromosomes is normal. Many clinical conditions and biochemical abnormalities (single gene disorders) are caused by defects in a single gene. A single gene disorder may be inherited in a number of different patterns:

1. Autosomal dominant, e.g. Waardenburg syndrome.
2. Autosomal recessive, e.g. oculocutaneous albinism.
3. X-linked recessive, e.g. haemophilia.

In addition, a single gene disorder may be due to a new mutation in the individual resulting in a single gene defect. Such individuals will not have a family history of that condition.

**SINGLE GENE DISORDERS ARE CLINICAL CONDITIONS RESULTING FROM DEFECTS IN A SINGLE GENE**

There three conditions are typical examples of single gene disorders with different patterns of inheritance. They illustrate many of the problems and management principles of caring for these individuals and their families.

The patterns of inheritance of single gene defects and other examples of these disorders are discussed further in Unit 51 of the Perinatal Education Programme.

**WAARDENBURG SYNDROME**

54-2 WHAT IS WAARDENBURG SYNDROME?

Waardenburg syndrome is an inherited disorder that is made up of a recognisable collection of clinical features including deafness. It is the commonest cause of congenital deafness associated with a known syndrome in southern Africa.

54-3 HOW IS WAARDENBURG SYNDROME INHERITED?

Waardenburg syndrome is an **autosomal dominant** disorder:

1. About two thirds of individuals with Waardenburg syndrome have inherited the abnormal dominant gene, and therefore the condition, from an affected parent.
2. The remaining third of people with Waardenburg syndrome have the condition as the result of a new gene mutation. Therefore, neither of their parents carries the abnormal gene.

*** The new gene mutation for Waardenburg syndrome is associated with advanced paternal age (having a father older than 55 years) at the time of birth.

54-4 HOW COMMON IS WAARDENBURG SYNDROME?

Waardenburg syndrome occurs in about 1 in 30 000 people in all populations.

In southern Africa approximately 4% of people with profound deafness have Waardenburg syndrome. This is similar to studies from other parts of the world where the prevalence varies from 2 to 5%.
54-5 WHAT ARE THE MAIN CLINICAL FEATURES OF PEOPLE WITH WAARDENBURG SYNDROME?

The main clinical features of Waardenburg syndrome are:

1. Very blue eyes (sapphire blue). The iris of both eyes can have this extraordinary blue colouring which is very noticeable in black Africans who usually have brown eyes. In some cases only one eye or part of the iris has this colouring and the other eye or part of the iris has the normal eye colour.
2. Eyebrows. The inner (medial) part of the eyebrows is very bushy and often the eyebrows meet in the middle.
3. Deafness. Sensory deafness is the most serious feature of Waardenburg syndrome. It usually involves both ears and is severe. Deafness is found in 25 to 50% of people with Waardenburg syndrome.
4. A white forelock. Between 30 and 40% of people with Waardenburg syndrome have a white or grey patch of hair in the middle and front of their heads. This may vary from a small area that is not very obvious to a large striking white forelock of hair.
5. Early greying of hair and eyebrows. This begins in the twenties in some people with Waardenburg syndrome.
6. Partial albinism. About 20% of people with Waardenburg syndrome have patches of skin with less or no pigmentation.

INDIVIDUALS WITH WAARDENBURG SYNDROME ARE TYPICALLY DEAF WITH A CHARACTERISTIC WHITE FORELOCK

See the photographs of individuals with Waardenburg syndrome at the end of the unit.

*** Some people with Waardenburg syndrome may also have noses with a round, upturned tip with the sides being underdeveloped, full lips and a prominent lower jaw.

*** There are considered to be two main forms of Waardenburg syndrome, types I and II, both of which have similar features but which can be told apart because type I has dystopia canthorum and type II does not. Dystopia canthorum is the name given to the facial feature in which the inner corners (canthi) of each eye are further apart than normal and the nasal bridge is broad. Careful examination of the lower eyelid will also show that the openings to the tear ducts (lacrimal puncta) are further away from the inner corners of the eye than usual. Deafness is found in 25% of people with type I and 50% of people with type II Waardenburg syndrome. In southern Africa, type I is found in over 50% of people with Waardenburg syndrome.

54-6 MUST A PERSON HAVE ALL THESE FEATURES TO BE DIAGNOSED WITH WAARDENBURG SYNDROME?

No. Three or more of the main features must be present to consider the clinical diagnosis. In Waardenburg syndrome, as is found in many other syndromes, the number and severity of the clinical features present can vary greatly. This is called variation in expression of the syndrome.

54-7 IS THERE A TEST TO CONFIRM THE DIAGNOSIS OF WAARDENBURG SYNDROME?

Yes. The gene for Waardenburg syndrome can be tested to confirm the diagnosis. However the test is expensive and presently not undertaken in South Africa.
54-8  WHAT ARE THE MAJOR COMPLICATIONS OF WAARDENBURG SYNDROME?

1. Deafness and the problems associated with this, including lack of speech and communication ability, schooling problems and social stigmatisation.
2. Recurrent eye infections in infants and children caused by the problems with the tear ducts.

54-9  ARE PEOPLE WITH WAARDENBURG SYNDROME INTELLECTUALLY DISABLED?

No. However, infants and children with deafness from any cause, including Waardenburg syndrome, are often considered to be developmentally delayed. This is because of the lack of speech and inability to communicate. If the problem is discovered early and appropriate therapy started, many of the developmental problems may be overcome and the person is shown to have normal intelligence.

54-10 WHAT CARE IS AVAILABLE FOR PEOPLE WITH WAARDENBURG SYNDROME?

1. Early diagnosis:

   In people with Waardenburg syndrome, as with all cases of infant and childhood deafness, it is very important to diagnose their deafness as early as possible to ensure they can start early with intervention programmes. This will ensure the best long-term outcome for the person’s communication ability. The early clinical confirmation of the diagnosis of Waardenburg syndrome is also important so that genetic counselling can be offered to the family.

2. Managing the deafness:

   The early diagnosis of deafness, in infancy if possible, is important as it means speech and communication therapy can be started early ensuring the best long-term results. Assessment to find out if hearing aids may benefit the infant or child should also be done as early as possible. For this treatment the infant or child needs to be seen at a specialised centre. On-going day to day speech therapy in areas far from such centres may be made possible for infants and young children with the help of community-based rehabilitation workers. However, to achieve the best results, these children will need to attend centres for specialised training and eventually need to go to schools for the auditory disabled (deaf).

3. Manage repeated eye infections:

   Conjunctivitis needs to be treated with repeated swabbing of the eye with clean water (boiled and then cooled), massaging the tear duct, and antibiotic drops or ointment if indicated. If the problem recurs often then surgical probing of the tear duct can be performed.

4. Genetic counselling and psychosocial support.

54-11 WHAT GENETIC COUNSELLING IS NEEDED BY PARENTS WHO HAVE A CHILD WITH WAARDENBURG SYNDROME?

Genetic counselling is a major part of the care of people with Waardenburg syndrome and their family, especially the parents. The parents need to be educated and informed about:

1. The diagnosis.
2. The cause of Waardenburg syndrome. That Waardenburg syndrome is a genetic disorder, inherited in an autosomal dominant manner.
3. What Waardenburg syndrome means for the affected person and what can be done to treat the various problems.

PERINATAL EDUCATION PROGRAMME
4. The risks for parents with a child with Waardenburg syndrome having a child with Waardenburg syndrome in future pregnancies and their options for reducing this risk and preventing the birth of another affected child.

The parents, family and child with Waardenburg syndrome need to be offered on-going psychosocial support as with all individuals who have a congenital disability. There is presently no support group for Waardenburg syndrome in South Africa.

54-12 WHAT IS THE RISK FOR PARENTS OF A CHILD WITH WAARDENBURG SYNDROME HAVING AFFECTED CHILDREN IN FUTURE PREGNANCIES?

To assess this risk, the parents have to be examined to see if one of them has signs of Waardenburg syndrome. Because of variation of expression of the syndrome it may not have been diagnosed in one of them, as their symptoms and signs may not have been as severe or numerous as in their child. For example, an affected parent may not necessarily be deaf.

If a parent is diagnosed with Waardenburg syndrome, then all future children of that parent have a 1 in 2 (50%) risk of having Waardenburg syndrome. These children with Waardenburg syndrome, when they have grown up and have their own children, will also have a 1 in 2 (50%) risk of passing the syndrome to each of their offspring. This is typical of an autosomal recessive disorder.

If both parents of a child with Waardenburg syndrome are normal, then the cause of Waardenburg syndrome in the child is due to a new mutation. Future children of that couple will have only a very small risk of being affected with Waardenburg syndrome.

54-13 CAN WAARDENBURG SYNDROME BE PREVENTED?

Yes. Because the genes for Waardenburg syndrome are known, it is possible to do prenatal diagnosis. However, as the test is not presently offered in South Africa, prenatal diagnosis of Waardenburg syndrome is not practical.

OCULOCUTANEOUS ALBINISM

54-14 WHAT IS ALBINISM?

Albinism is an inherited condition. The clinical signs and symptoms of albinism are caused by a lack of melanin in the cells of the body. Melanin is the pigment that gives colour to the skin, hair and eyes.

*** Of interest, albinism occurs in many animals such as the white lions of Timbavati.

54-15 WHAT IS OCULOCUTANEOUS ALBINISM?

There are different forms of albinism:

1. Albinism with a lack of pigment in the eye (oculo-) plus skin (cutaneous) and hair. This is called oculocutaneous albinism or OCA.
2. Albinism which only affects the eyes and not skin or hair. This is called ocular albinism.
*** Oculocutaneous albinism (OCA) is further classified into types I and II. In sub-Saharan Africa, including South Africa, oculocutaneous albinism type II is the most common form of albinism found.

54-16 HOW IS OCULOCUTANEOUS ALBINISM INHERITED?

OCA is inherited as an **autosomal recessive** condition. Therefore, a person affected with OCA has received two copies of the abnormal gene (homozygous) that is responsible for melanin production (i.e. one abnormal gene from each parent). As a result, the cells of an affected individual are unable to produce normal amounts of pigment and, therefore, they are very pale.

Each parent of an affected individual has one normal and one abnormal copy of the pigment gene (i.e. is heterozygous). Because they have one normal gene that can produce melanin, they have normal pigmentation and do not show signs of OCA.

**OCULOCUTANEOUS ALBINISM IS INHERITED AS AN AUTOSOMAL RECESSIVE DISORDER**

54-17 HOW COMMON IS OCULOCUTANEOUS ALBINISM?

Oculocutaneous albinism is common and is the commonest single gene disorder in South Africa where the overall prevalence of OCA in the Black population is 1 in 4000. However it is even higher in those communities that accept intermarriage (consanguinity) as part of their culture (e.g. the Venda, Tswana, Pedi and Southern Sotho peoples). The population prevalence of OCA in other ethnic groups in South Africa is not known.

*** The population prevalence of OCA is similar throughout most of sub Saharan Africa, varying between 1 in 4000 to 5000 people. The highest prevalence, 1 in 1000, is found in the isolated Batonka people who live in the Zambezi River valley. In contrast, in Europe, the prevalence of OCA varies between 1 in 10 000 and 20 000.

**OCULOCUTANEOUS ALBINISM IS THE COMMONEST SINGLE GENE DISORDER IN SOUTH AFRICA**

54-18 WHAT ARE THE MAIN CLINICAL FEATURES OF OCULOCUTANEOUS ALBINISM?

People affected with OCA have normal physical and facial features, but have markedly decreased pigmentation of their skin, hair and eyes resulting in all these features being pale. Black people with OCA are, therefore, easily recognised. In White people, OCA is less obvious. The features of OCA are:

1. **Skin:**

   They have pale skin which is very sensitive to sunlight.

   *** They may have small spidery pigmented patches called ephelides scattered over their bodies, mainly on sun-exposed areas such as the arms and faces.

2. **Hair:**

   A black African with OCA usually has pale or corn-coloured hair. The hair colour in a few individuals may be brown or reddish (rufous).
3. **Eyes:**

Black African people with OCA have brown eyes, but their eyes may be lighter brown than normal. They have numerous eye problems.

See photographs of individuals with oculocutaneous albinism at the end of this unit.

**54-19 WHAT EYE PROBLEMS ARE COMMON IN PEOPLE WITH OCULOCUTANEOUS ALBINISM?**

2. They all have nystagmus. This consists of jerky movements of the eyes in a horizontal or vertical direction or both.
3. Most have poor vision (96%). About two-thirds are short sighted (myopia) and a third long sighted (hyperopia).

**ALL PEOPLE WITH OCULOCUTANEOUS ALBINISM HAVE PROBLEMS WITH THEIR EYESIGHT**

*** Most have astigmatism (92%) and poor depth judgement. People with OCA also have abnormal visual pathways as the gene for melanin production is also responsible for the development of the optic nerve tracks from the eye to the visual centre at the back of the brain. Because of their abnormal visual pathways they do not have binocular vision like normal people.

**54-20 WHAT ARE THE MAJOR COMPLICATIONS OF OCULOCUTANEOUS ALBINISM?**

1. **Skin:**

Normally, melanin prevents the sun’s ultraviolet rays being absorbed by the skin. If melanin is not present in adequate amounts, the ultraviolet rays in sunlight penetrate and damage the skin. Problems resulting from a lack of pigmentation in the skin include:

(i) Easy sun-burning and blistering.
(ii) Rapid ageing of the skin which leaves it thin, dry and it is easily damaged. These areas of skin often become infected.
(iii) Skin cancer (squamous cell carcinoma). People with OCA are at high risk of developing cancer of the skin on sun exposed areas, especially if the person does not take precautions to protect themselves from the sun. People living nearer the equator, where the sunlight is stronger, are at a higher risk.
(iv) Early death from skin cancer is a serious risk for people with OCA.

2. **Eyes:**

(i) Lack of pigment in the eyes can result in sunlight-induced damage to the eyes. This will cause a further worsening in visual ability
(ii) As individuals with OCA have abnormal eyesight, they may experience school learning difficulties and job discrimination in later life.

3. **Social stigmatisation:**

(i) People with OCA in Africa look very different from the rest of the population.
(ii) Throughout Africa, myths or legends regarding the birth, life and death of people with OCA are common. These myths can affect people’s attitude to people with OCA, mostly negatively but in some populations positively. Therefore, in many regions of sub Saharan Africa there is isolation and stigmatisation of people with OCA.
Research from South Africa indicates that people with OCA are now generally well accepted in the community, and they in turn appear to be reasonably well adjusted. Myths regarding people with OCA are however plentiful, and it has been reported that mothers of newborns with OCA experience problems bonding with their babes and may suffer from depression, similar to that described by mothers with other birth defects.

**SKIN CANCER IS A COMMON COMPLICATION OF OCULOCUTANEOUS ALBINISM**

54-21 WHAT ARE SOME OF THE SOUTH AFRICAN MYTHS REGARDING PEOPLE WITH OCULOCUTANEOUS ALBINISM?

1. **Birth myths:**

These are used to try and explain the unexpected birth of an infant with OCA. They include that the birth is a punishment for some supposed bad deed committed by the parent(s); that the mother conceived during menstruation; that the mother must have come into contact with a person with albinism during pregnancy; that the mother ate an excess of certain foods or had an infection during pregnancy.

2. **Life myths:**

These are about special qualities that people with OCA supposedly have. One of the common beliefs is that people with OCA may have special religious, spiritual or supernatural power. People with OCA are often considered either very intelligent or intellectually disabled.

3. **Death myths:**

The death of people with OCA is surrounded with superstition. It is widely believed that they do not die, but rather disappear or vanish.

54-22 ARE CHILDREN WITH OCULOCUTANEOUS ALBINISM INTELLECTUALLY DISABLED?

No. Children with OCA generally have a normal intelligence and are not intellectually disabled. Due to their visual disability, infants and young children may present with evidence of developmental delay. Older children may have schooling problems due to their poor vision or psychosocial problems. However, if these problems are recognised early and correctly managed with eye and visual care, early intervention programmes and counselling, they can be overcome.

54-23 WHAT IS THE LIFE EXPECTANCY OF CHILDREN WITH OCULOCUTANEOUS ALBINISM?

The life expectancy of people with OCA should be similar to that of normal people. However, due to the high risk of developing skin cancer, many unfortunately die in early adult life if not correctly managed. In Tanzania and Nigeria, countries in the tropics and close to the equator, only 10% of people with OCA live longer than 30 years. No figures on life expectancy are currently available for South Africa. However, it is considered to be better than the figure for Tanzania and Nigeria as South Africa is mostly outside of the tropics.

**MANY PEOPLE WITH OCULOCUTANEOUS ALBINISM DIE OF SKIN CANCER**

**PERINATAL EDUCATION PROGRAMME**
54-24 WHAT IS THE CORRECT CARE FOR PEOPLE WITH OCULOCUTANEOUS ALBINISM?

1. Early clinical diagnosis:

The first step in caring for people with OCA is to make an early, correct diagnosis. OCA is a clinical diagnosis and is usually made at the birth of the infant, especially in the black African infants in whom the diagnosis is very obvious. However, the clinical signs can be more difficult to recognise in White or Asian infants.

2. Good skin and eye care:

Good skin and eye care is essential to prevent skin cancer and progressive loss of eyesight.

3. Neurodevelopmental therapy, special education and rehabilitation:

This should be provided in the community, if possible, to enable these children to learn and develop normally.

4. Genetic counselling and psychosocial support.

54-25 WHAT SKIN CARE IS NEEDED FOR CHILDREN WITH OCULOCUTANEOUS ALBINISM?

It is essential for people with OCA to reduce their exposure to sunlight to the greatest extent possible. As it is not possible for a person with OCA to remain out of the sun continually, when they do go out they should wear clothes to cover as much skin as possible, i.e. long trousers or skirts, long sleeved tops or shirts, and hats with wide brims.

Sun exposed skin, especially hands, arms and face, should be covered with cream containing sunscreen (sun barrier creams). Cream with sun protection factor (SPF) of 30 or greater must be used. Moisturising cream should be used on dry, cracking or chaffed skin, and skin infection should be treated vigorously with antiseptics and antibiotics if clinically indicated. Unfortunately many clinics do not have sun barrier creams. They are expensive to buy.

Adolescents and adults with OCA should be aware of the dangers of skin cancer. They should be taught how to recognise areas of skin cancer so that they know what to look for to be able to suspect and possibly diagnose cancer as early as possible (e.g. sores that do not heal). In addition they should have yearly examinations to exclude the development of skin cancer.

GOOD SKIN PROTECTION AGAINST SUNLIGHT IS ESSENTIAL TO PREVENT SKIN CANCER

54-26 WHAT EYE CARE IS NEEDED FOR CHILDREN WITH OCULOCUTANEOUS ALBINISM?

People with OCA need to protect their eyes from the harmful effects of sun and bright light by avoiding it where possible and wearing protective eyewear (appropriate dark glasses) and broad brimmed hats. In this way, further damage to their visual disability can be minimised.

All people with OCA should have regular ophthalmic or optometric assessments from infancy. This is necessary to ensure they obtain the correct glasses and treatment for their individual problems from early life, thus giving them the best chance of normal vision and making sure that their sight is not damaged by the lack of eye care.
GOOD EYE CARE AND THE CORRECT DARK GLASSES ARE ESSENTIAL TO PROTECT EYE SIGHT

54-27 WHAT NEURODEVELOPMENTAL THERAPY, COMMUNITY BASED REHABILITATION AND SPECIAL EDUCATION IS NEEDED FOR CHILDREN WITH OCULOCUTANEOUS ALBINISM?

1. In infants and children with severe visual disability it may be necessary for them to receive neurodevelopmental therapy, e.g. occupational therapy at their local hospital.
2. If specialised therapy is not available in their area they will have to rely on local community based rehabilitation services.
3. When children with OCA reach school going age, decisions will need to be made regarding school placement. Where possible, children with OCA should be encouraged to attend normal schools. Efforts to assist them in a normal school may be necessary, e.g. placement in the front row of the class. If however their visual disability is too severe, then scholars may need to be placed in a school for the visually disabled.

54-28 WHAT GENETIC COUNSELLING IS NEEDED FOR FAMILIES WITH OCULOCUTANEOUS ALBINISM?

Genetic counselling is a major part of the care of people with OCA and their family, especially their parents. The parents need to be educated and informed about:

1. The diagnosis, which is a clinical one and is usually obvious.
2. The cause of OCA. To explain that OCA is a genetic disorder, inherited in an autosomal recessive manner. This information can be used to try and dismiss the myths about why an infant with OCA is born to a couple.
3. What OCA means for the affected person, what can be done to prevent and manage the various problems. It is essential to stress that every effort must be made to avoid direct sunlight on the skin and in the eyes by not spending a lot of time in the sun, wearing the proper clothes and protective eyewear and using sunscreen cream.
4. The risks for normal parents with an OCA infant having another child with OCA in future pregnancies. Their options for reducing the risk of having another infant with OCA should be discussed.

The parents, family and person with OCA need to be offered on-going psychosocial support.

54-29 WHAT IS THE RISK FOR NORMAL PARENTS OF A CHILD WITH OCULOCUTANEOUS ALBINISM HAVING OTHER AFFECTED CHILDREN IN FUTURE PREGNANCIES?

OCA is an autosomal recessive condition. As carriers of a single abnormal OCA gene, parents of a child with OCA have a 1 in 4 risk (25%) of having a further affected child in every future pregnancy. With another partner, the chance of either parent having an affected child is very small.

54-30 HOW CAN OCULOCUTANEOUS ALBINISM BE PREVENTED?

The gene for OCA has been identified and, therefore, it is possible to offer prenatal diagnosis for OCA to parents who both carry the abnormal gene. This can only be done after the parents receive genetic counselling. Genetic counselling is ideally undertaken before conception, or in the first 10 weeks of the pregnancy. The prenatal gene test is done on fetal cells obtained by amniocentesis at 16 weeks. Once the result of the prenatal test is available, further genetic counselling will be necessary to discuss these results.
54-31 WHY DO PEOPLE WITH OCULOCUTANEOUS ALBINISM, AND THEIR FAMILY, NEED PSYCHOSOCIAL SUPPORT?

People with OCA, as with all individuals who have a congenital disability, suffer lifelong problems which require lifelong care. The burden of the disorder is experienced not only by the affected person, but also the family, especially parents, brothers and sisters. Mothers of newborns with OCA need psychosocial support to help them accept and bond with their infant, and overcome possible depression. In addition, the problem is genetic and thus there is the possibility for the parents, the affected person and other family members to also have children affected with OCA. Support, help and reassurance in these circumstances may be a lifelong need.

54-32 WHO CAN OFFER PSYCHOSOCIAL SUPPORT?

Professional psychosocial support can be obtained from:

1. Doctors, nurses (especially genetic trained nursing staff), genetic counsellors and neurodevelopmental therapists.
2. Social workers.
3. Patient/parent support groups. These groups play a vital role in offering information and support to people affected with congenital disability.

There is a strong support group for people with OCA in South Africa, the Albinism Society of South Africa (ASSA), P.O. Box 9881, Johannesburg, 2000. (Tel: 011- 838-6529).

HAEMOPHILIA

54-33 WHAT IS HAEMOPHILIA?

Haemophilia is an inherited, lifelong bleeding disorder which affects mainly males.

There are two types of haemophilia, haemophilia A and haemophilia B. Haemophilia A (classical haemophilia) is the common form of haemophilia. Both types present clinically as a bleeding problem.

54-34 WHY DO PATIENTS WITH HAEMOPHILIA BLEED EXCESSIVELY?

Haemophilia A is caused by a lack of clotting factor VIII (eight) while haemophilia B is caused by a lack clotting factor IX (nine).

*** It is the low level of function, rather than a low concentration of the clotting factor in the blood, which results in an increased tendency to bleed. The single gene defect results in the formation of a defective clotting factor, which does not function normally.

54-35 HOW IS HAEMOPHILIA INHERITED?

Both types of haemophilia are inherited as X-linked recessive disorders. There are separate single gene defects for haemophilia A and haemophilia B on the X chromosome.

A woman with a haemophilia gene (i.e. an abnormal gene) on only one X chromosome is a carrier (i.e. she is a heterozygote). Because she has a normal gene on her other X chromosome, she will still be able to produce enough clotting factor. If she passes the X chromosome containing the abnormal gene on to her daughter, then her daughter will also be a carrier.
If a son inherits the X chromosome with the haemophilia gene from his mother, he will have haemophilia as his short Y chromosome does not have the gene to produce the clotting factor.

**HAEMOPHILIA IS INHERITED AS AN X-LINKED RECESSIVE CONDITION. THEREFORE, WOMEN CARRY THE ABNORMAL GENE AND THEIR SONS ARE AT RISK OF HAVING HAEMOPHILIA**

**54-36 CAN FEMALES HAVE HAEMOPHILIA?**

Yes. About 10% of female carriers have signs of mild haemophilia. All patients with moderate or severe haemophilia are males.

*** If a daughter inherits a haemophilia gene from her carrier mother and another from her haemophiliac father, both her X chromosomes will contain the abnormal gene and she will have haemophilia. This is rare.

**54-37 HOW COMMON IS HAEMOPHILIA?**

1. Haemophilia A occurs in approximately 1 in 5000 males throughout the world.
2. Haemophilia B occurs in approximately 1 in 40 000 males throughout the world.

In South Africa, haemophilia A has been found in 1 in 5000 white males but only 1 in 20 000 black males. Due to poor socioeconomic conditions and inadequate access to health care in many black communities, some black people with haemophilia A may not be diagnosed and registered. Others may die very young with severe bleeding without the diagnosis being made. Therefore the population prevalence may be less than expected.

**54-38 WHAT ARE THE MAIN CLINICAL FEATURES OF PEOPLE WITH HAEMOPHILIA?**

People with haemophilia present with excessive bleeding, involving skin and mucous membranes (bruising), muscle, joints, internal organs or brain. Infants usually bleed into soft tissues while older boys usually bleed into joints.

The severity and frequency of bleeds depends on the concentration of clotting factors VIII and IX in the patient’s blood:

1. People with mild haemophilia only have 5 to 35% of the normal factor VIII or IX level. They usually only bleed following severe trauma and at surgery. Because bleeding is not a major problem they may only be diagnosed later in life.
2. People with moderate haemophilia have between 1 and 5% of the normal factor VIII or IX level and they bruise easily. They usually bleed excessively following trauma, surgery or dental care but rarely have spontaneous bleeds. They usually do not have serious problems with bleeding into joints. They should be able to be diagnosed before the age of 5 years.
3. People with severe haemophilia have less than 1% of the normal factor VIII or IX level and may bleed spontaneously or with minimal trauma. They can bleed in any part of the body but some parts such as the large joints (knees, ankle and elbow) are more prone to injury and bleeding. They should be diagnosed in the first year of life.

Bleeding is unusual in newborns but infants with haemophilia can bleed from circumcision sites. Infants with severe haemophilia will bleed into muscles from injection or needle stick sites or spontaneously into cephalhaematomas or within the skull (intracranial bleed).

See the photographs of individuals with haemophilia at the end of the unit.

PERINATAL EDUCATION PROGRAMME
54-39 ARE THERE TESTS TO CONFIRM THE DIAGNOSIS OF HAEMOPHILIA?

Yes. If haemophilia is suspected, the following tests can be done to confirm the diagnosis:

1. Partial thromboplastin time (PTT). This is prolonged in people with moderate and severe haemophilia. However, it can be normal in people with mild haemophilia.
2. Clotting factor VIII levels are low in people with haemophilia A while clotting factor IX levels are low in people with haemophilia B.
3. Gene (DNA based) tests. The genes for haemophilia A and B are known and can be tested for in South Africa. The test is expensive and not simple, and therefore is only used in special circumstances, including prenatal diagnosis, testing for carriers and confirming a diagnosis.

54-40 WHAT ARE THE MAJOR COMPLICATIONS OF HAEMOPHILIA?

These relate to the severity and site of bleeding. A person with haemophilia may have bleeding problems in any part of the body. Major bleeds can cause death or disability and they require immediate treatment with the correct clotting factor. Minor bleeds also require treatment and, depending on their position, may cause complications.

Sites into which bleeding occurs include:

1. Joints:

Joint bleeds (haemarthrosis) into the knees, elbows and ankles are common and are the most disabling complication of severe haemophilia. Joint bleeds present with pain, swelling, stiffness and refusal to move that limb. Treatment must be started with the correct clotting factor every 12 to 24 hours, and the joint must be splinted. Ice packs can be used to lessen the swelling. Failure to effectively treat these bleeds will eventually result in affected joints becoming fixed and not able to move due to the damage that the blood causes in the joint. Arthritis can develop. Physical disability resulting from joint damage is a major problem for people with haemophilia in developing countries.

2. Muscle and soft tissues:

Bleeding into muscles and soft tissues (such as the neck and throat) may be life threatening and need immediate treatment with clotting factors. Bleeding into muscle is very painful and can be dangerous. If not managed properly it can result in pressure on nerves leading to nerve damage with paralysis and wasting of limbs.

Cuts of the mouth and tongue, tooth extractions and nose bleeds may ooze for long periods and require treatment.

3. Internal bleeding:

Bleeding into the organs of the abdomen and chest is less common but may be spontaneous and serious. Abdominal pain in a boy with haemophilia always suggests a bleed. Intracranial bleeding can be spontaneous or result from minor trauma, often not recognised in a child. Intracranial bleeding presents as headache, vomiting, and lethargy or irritability. Urgent clotting factor replacement is needed with internal bleeding.
54-41 WHEN SHOULD THE CLINICAL DIAGNOSIS OF HAEMOPHILIA BE SUSPECTED?

The diagnosis of haemophilia should be suspected if a male presents with:

1. Large cephalhaematoma or unexplained intracranial bleeding in newborns.
2. Excess bleeding from circumcision.
3. Prolonged or repeated nose bleeding, and especially if it is from both nostrils.
4. Prolonged oozing or renewed bleeding after mouth injury or tooth extraction.
5. Easy and excessive bruising, especially if a firm subcutaneous lump is felt with the bruise.
7. Haemarthrosis (bleeding into joints).
8. Prolonged oozing or renewed bleeding after surgery or trauma.

A female carrier with mild haemophilia may be suspected if she has a close male relative (brother, son or maternal uncle) with haemophilia and presents with heavy periods (menorrhagia), easy bruising or bleeding after trauma, surgery or childbirth.

It is suspected that the diagnosis of haemophilia is being missed in many cases in South Africa. Correct diagnosis of haemophilia is needed to be able to give the correct treatment and genetic counselling. A PTT test can be used to confirm that the bleeding is due to a lack of one of the clotting factors.

*** Blood for a PTT test must be drawn in a Vacutainer tube with a blue top and must be kept cool and reach the laboratory within a few hours.

54-42 WHAT IS THE TREATMENT OF BLEEDING DUE TO HAEMOPHILIA?

Bleeding is rapidly controlled by giving intravenous factor VIII concentrate in haemophilia A and factor IX concentrate in haemophilia B. This reduces pain and lowers the risk of developing serious complications, especially chronic joint disease. For major bleeds, clotting factors should be given in hospital. However, patients over two years of age can often be treated at home.

Where possible, children with severe haemophilia are now being given prophylactic home therapy with clotting factor three times a week to prevent bleeding episodes from occurring.

Once factor VIII or IX concentrate has been given further treatment of the problems may be needed, such as splinting during recovery, and physiotherapy to help preserve movement in the recovery phase. All operations need to take place under the cover of clotting factor replacement to ensure that there will be no excessive bleeding.

Never give aspirin or non-steroidal anti-inflammatory drugs (e.g. Voltaren and Indocid) to someone with haemophilia as these drugs increase the risk of bleeding. Haemophilia is a serious condition and must be managed in partnership with a provincial haemophilia treatment centre.

As soon as bleeding is suspected in someone with haemophilia, immediate treatment with the correct clotting factor concentrate must be started.

*** Vasopressin given nasally or intravenously increased the level of factor VIII and is useful in treating mild haemophiliacs. Tranexamic acid (Cyklokapron) can be added to the clotting factor infusion to help maintain clots in bleeding from the mouth, nose or tooth sockets.
54-43 WHAT GENETIC COUNSELLING IS NEEDED BY PEOPLE WITH HAEMOPHILIA AND THEIR FAMILIES?

Genetic counselling is an important part of the care of people with haemophilia, and their families. All need to be educated and informed on:

1. **The diagnosis:** The clinical features and the blood tests to confirm the diagnosis.
2. **The pattern of inheritance:** About 80% of males with haemophilia have a mother who is a carrier of the single gene defect on one of her X chromosomes. About 10% of these carrier mothers have mild symptoms and signs of haemophilia. The 20% of males with haemophilia, who do not have carrier mothers (no family history of bleeding), have a new mutation of their haemophilia gene.
3. **What care is needed:** What haemophilia means for the affected person and what can be done to treat the various problems.
4. **Risks for future children also having haemophilia:** Parents of a child with haemophilia need to understand the risk of having another child with haemophilia. They must also be told about their options and possibilities for reducing this risk and preventing the birth of another affected child. The parents also need to know of the risk that their daughters will inherit the abnormal gene from their mother, and also become a carrier. They need to understand what this will mean for the daughters.

54-44 WHERE CAN PATIENTS WITH HAEMOPHILIA AND THEIR PARENTS GET HELP?

The parents, family and child with haemophilia need to be offered on-going psychosocial support as they have problems which require lifelong care. The burden of the disorder and the care is experienced not only by the affected person, but also the family, especially parents, brothers and sisters. Support, help and reassurance in these circumstances may be obtained from:

1. Doctors, nursing staff (especially haemophilia and genetic trained nursing staff), genetic counsellors, physiotherapists and social workers.
2. A Patient/Parent support group. These groups play a vital role in offering information and support to people affected with congenital disability. There is presently a very strong haemophilia support group in South Africa.


54-45 WHAT IS THE RISK FOR PARENTS, WITH A SON WITH HAEMOPHILIA, HAVING AFFECTED SONS IN FUTURE PREGNANCIES?

If the mother is a carrier of the abnormal gene then in each of her future male pregnancies she will have a 1 in 2 (50%) chance of having a son affected with haemophilia.

If the mother is NOT a carrier of an abnormal haemophilia gene then her risk for having another son with haemophilia is very small.
*** With no family history of haemophilia, it has recently been shown that the mother may be a carrier, having inherited a new mutation from her elderly father.

54-46 WHAT IS THE RISK FOR PARENTS, WITH A SON WITH HAEMOPHILIA, HAVING HAEMOPHILIA CARRIER DAUGHTERS?

The risk is 1 in 2 (50%). This is the same as the risk of having an affected son. The carrier mother will give her X chromosome with the abnormal gene to half of her children. The carrier daughters, like their mothers, have the same risks (50%) of passing the abnormal haemophilia gene on to their sons and daughters.

54-47 HOW CAN YOU FIND OUT WHETHER THE MOTHER OF A CHILD WITH HAEMOPHILIA IS A CARRIER?

If a couple has a son with haemophilia, then it is important to find out if his mother is a carrier of an abnormal haemophilia gene. There are two ways of finding this out:

1. If the mother of the affected son has one other affected male member in her close family, such as a brother or uncle, then she is almost certainly a carrier of the abnormal gene for haemophilia.
2. If the mother does not have such an affected close relative then she or her son with haemophilia may have a new mutation for the abnormal gene. The best way then to find out if the mother is a carrier of the abnormal gene is to send blood from her and her son for the gene (DNA) test.

54-48 CAN A FATHER WITH HAEMOPHILIA HAVE AFFECTED CHILDREN?

Men have one X and one Y chromosome. If a man has haemophilia he will have an abnormal haemophilia gene on his X chromosome but not on his Y chromosome (i.e. an X-linked recessive disorder). When he has children he gives his Y chromosome, with the no haemophilia gene, to his sons who will get their X chromosome from their mother. Therefore, if the mother is not a carrier of an abnormal haemophilia gene, their sons will not have haemophilia.

He will give his X chromosome, with the abnormal haemophilia gene, to his daughters who will all, therefore, be carriers of the abnormal haemophilia gene.

54-49 CAN HAEMOPHILIA BE PREVENTED?

Yes. Because the abnormal gene for haemophilia can be tested for, a woman who is a carrier of this abnormal gene can be offered prenatal diagnosis. This is done after she and her partner have been given genetic counselling.

It is best to provide genetic counselling and to determine whether the woman is a carrier before she falls pregnant. Prenatal diagnosis can also be done early in pregnancy. This is carried out by obtaining fetal cells by amniocentesis, and testing these cells to see if they have an abnormal haemophilia gene (A or B).

*** The cells of the placenta can be obtained by chorionic villous biopsy, even earlier in pregnancy. The fetus and placenta have the same genes.
54-50 WHAT SPECIAL CIRCUMSTANCES MUST BE CONSIDERED IN HAEMOPHILIA?

1. If a woman is suspected of being a carrier of a haemophilia gene, the diagnosis must be confirmed or excluded before she becomes pregnant or as early in the pregnancy as possible. This allows for genetic counselling and the option of prenatal diagnosis to be offered. Ten percent of carriers may bleed heavily during a normal delivery or caesarean section. There is also a small risk (1-2%) of a male fetus, affected with severe haemophilia, having an intracranial bleed with a vaginal delivery. Women who are known carriers, or at risk of being carriers, of an abnormal haemophilia gene should be referred to a haemophilia treatment centre before and during pregnancy.

2. In infants suspected of having haemophilia, circumcision should not be done and they should not be given intramuscular injections. Immunisations can be given subcutaneously. They must be referred for diagnostic tests.

3. People with haemophilia should avoid medications that may cause bleeding. The most common and important of these is aspirin and the other non-steroidal (anti-inflammatory) analgesics (pain killers). Paracetamol (Panado) can be used.

CASE PROBLEMS

CASE 1.

A woman with Waardenburg syndrome delivers her first born infant who also has a white forelock. She asks whether all her infants will have the same problem.

1. **What are the main features of Waardenburg syndrome?**

Very blue eyes, bushy eyebrows, deafness (25 to 50%) and a white forelock (30 to 40%). Premature greying of the hair and partial albinism is common.

2. **How is Waardenburg inherited?**

It is usually inherited as an autosomal dominant disorder. This woman’s child has inherited her dominant gene for Waardenburg syndrome. Each of her future children will have a 50% chance of inheriting the condition.

3. **Is there always a family history of the condition if a child presents with the features of Waardenburg syndrome?**

No. As with many autosomal dominant disorders, the condition may appear as a new mutation and will not be inherited from a parent. About a third of patients with Waardenburg syndrome do not have a family history of the condition.

4. **What is the main complication of Waardenburg syndrome?**

Severe sensory deafness affecting both ears. As a result they often have speech difficulties which affects their schooling and socialisation. They are not intellectually disabled.

5. **How common is Waardenburg syndrome in South Africa?**

It is not common (about one in 30 000 people). However, about 4% of people with severe deafness have the condition.
CASE 2.

The first born infant of black parents has very pale skin and hair with light brown eyes. They notice that the child has abnormal eye movements and appears to have poor vision. The nurse at the local clinic tells them that they should use skin cream on the infant to prevent sunburn. The clinic does not have sun protection cream and the parents cannot afford to buy the cream.

1. **What is the likely diagnosis in this infant?**

The infant probably has oculocutaneous albinism (OCA) as there is lack of pigment in the skin, hair and eyes. This is the common form of albinism in southern Africa.

2. **Are eye problems common in this condition?**

Yes. All people with OCA have eye problems and almost all have poor vision. This infant has the typical jerky eye movements known as nystagmus.

3. **Why is it important to use sun protection cream in these children?**

Because they lack adequate pigment (melanin) to protect the skin from the ultraviolet rays of the sun, they suffer severe skin damage. Sunburn and blistering are common, resulting in rapid aging of the skin.

4. **What skin complications should be looked for and treated?**

Infections and cancer.

5. **What is the life expectancy in people with oculocutaneous albinism?**

Many die young as a result of skin cancer. This emphasises the important of sun protection. The life expectancy of people with OCA in South Africa is not known.

CASE 3.

A woman, whose husband has oculocutaneous albinism, visits her general practitioner as they plan to start their family. She wants to know the risk of their children also being affected. She mentions that he gets upset as many people think he is intellectually disabled and some children are afraid of him.

1. **What is the pattern of inheritance in oculocutaneous albinism?**

It is inherited as an autosomal recessive disorder. Therefore, the father must have two abnormal genes for melanin production (homozygous). Each of his children will have a 50% chance of inheriting one of his genes containing the single gene defect for OCA. If the mother does not have this gene, then these children will appear normal but will be carriers (heterozygotes). It is possible to test the mother to see whether she is a carrier. If she is, then the couple should be sent for genetic counselling.

2. **How common is oculocutaneous albinism in South Africa?**

The prevalence in the black population is 1 in 3900, making it the commonest single gene disorder in the country. The prevalence in other ethnic groups is unknown.
3. **Are people with oculocutaneous albinism intellectually disabled?**

No. They have normal intelligence. However, their many eye problems results in poor vision and this may interfere with their schooling.

4. **Why may neighbouring children be afraid of someone with oculocutaneous albinism?**

Because people with oculocutaneous albinism look different. Children should not be afraid of people with oculocutaneous albinism as they are normal people except for their colouring. There are many myths about people with oculocutaneous albinism. In some communities these people are believed to have special powers.

5. **Can oculocutaneous albinism be prevented?**

The gene for OCA is known and, therefore, prenatal diagnosis is possible. Couples at risk of having a child with OCA should receive genetic counselling, preferably before they start a family.

---

CASE 4.

A newborn infant bleeds very heavily after circumcision. The mother reports that her uncle died of haemorrhage as a teenager after an operation, and that her brother is severely disabled due to repeated bleeds into his joints. She and her husband are well and have never had a bleeding problem.

1. **How does haemophilia present clinically?**

With excessive bleeding. Heavy bleeding after a circumcision is a typical way that haemophilia may present. Patients may bleed spontaneously or after trauma or surgery.

2. **Is repeated bleeding into joints a common way that haemophilia presents?**

Yes. Patients with severe haemophilia, who have less than 1% of the normal clotting factor activity, often bleed into big joints such as the knee, elbow or ankle. Repeated bleeds damages the joint resulting in pain and stiffness.

3. **Why do people with haemophilia bleed excessively?**

An inadequate amount of clotting factor VIII (in haemophilia A) or factor IX (in haemophilia B).

4. **How is haemophilia inherited?**

Both haemophilia A and B are inherited as X-linked recessive disorders. The females in the family carry the recessive gene on one of their X chromosome. Fifty percent of their male children will inherited the X chromosome with the abnormal gene, and as a result will have haemophilia. Both parents are usually clinically well without a bleeding problem although 10% of carrier mothers may have a mild problem.

5. **How is the diagnosis of haemophilia usually confirmed?**

The PTT (partial thromboplastin test) is abnormal and the concentration of either factor VIII (haemophilia A) or factor IX (haemophilia B) is low. The lower the concentration the more severe is the haemophilia. Haemophilia A is commoner than haemophilia B.

---

**PERINATAL EDUCATION PROGRAMME**
6. **How should a patient with a big bleed due to haemophilia be treated?**

The missing clotting factor should urgently be replaced by intravenous transfusion of factor VIII for haemophilia A and factor IX for haemophilia B. This is best done by immediate consultation with a haemophilia treatment centre.

**PHOTOGRAPHS OF CHILDREN WITH SINGLE GENE DISORDERS**

Picture 54-A: Infant with Waardenburg syndrome showing the white forelock of hair and pale eyes.

Picture 54B: Child with Waardenburg syndrome showing partial albinism, pale (sapphire blue) eyes and white eyebrows.
Picture 54-C: Mother with her child who has oculocutaneous albinism.

Picture 54-D: Infant with extensive bruising of the lower legs from Haemophilia.
Picture 54-E: Child with Haemophilia and haemarthrosis of the left elbow. Note the muscle wasting of the left upper arm and forearm, and the Medic Alert bracelet around his neck.
OBJECTIVES

When you have completed this unit you should be able to:

1. Define fetal alcohol syndrome.
2. Understand that alcohol can damage the fetus.
4. List factors which influence the blood alcohol concentration.
5. Recognise an infant with fetal alcohol syndrome.
6. Understand their pattern of growth and development.
7. Plan the care of an infant with fetal alcohol syndrome.
8. Understand the prevention of fetal alcohol syndrome.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way, nor may copies of the complete Programme be made, without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, however, parts of the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme are believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.

ISBN 0 7992 2254 2
55-1 WHAT IS FETAL ALCOHOL SYNDROME?

Fetal alcohol syndrome (FAS) is a clinical condition which presents with recognisable signs that include:

1. Abnormalities in appearance.
2. Delayed growth and development.

Fetal alcohol syndrome can usually be recognised at birth. It is a typical example of a birth defect caused by a teratogen.

FETAL ALCOHOL SYNDROME CAN USUALLY BE RECOGNISED AT BIRTH

55-2 WHAT IS THE CAUSE OF FETAL ALCOHOL SYNDROME?

Excessive drinking of alcohol by the mother during pregnancy.

*** Fetal alcohol syndrome is caused by exposure of the fetus to ethyl alcohol.

55-3 CAN FETAL ALCOHOL SYNDROME BE INHERITED?

No. Fetal alcohol syndrome is not a genetically inherited condition. It is caused by alcohol, i.e. a teratogen (something which damages the fetus). However there are often a number of individuals with fetal alcohol syndrome in a family (e.g. mother and child, or siblings) due to the excessive use of alcohol in that family.

55-4 IS FETAL ALCOHOL SYNDROME COMMON?

In some countries, such as South Africa, fetal alcohol syndrome is common. While one in a 1000 infants have fetal alcohol syndrome in most industrialised countries (e.g. USA, UK, France, Sweden), more than 50 per 1000 infants are affected in some communities in South Africa. This is one of the highest rates for fetal alcohol syndrome in the world.

*** In the Western Cape province of South Africa, the prevalence of fetal alcohol syndrome in children attending their first year of school is more than 50/1000, i.e. it is 30 times commoner than Down syndrome. In Soweto the incidence is 20/1000. These are very high rates.

55-5 WHICH COMMUNITIES HAVE A HIGH RATE OF FETAL ALCOHOL SYNDROME?

Fetal alcohol syndrome is most frequent in communities where poverty, low maternal education, unemployment and heavy drinking are common.

THE CAUSE OF FETAL ALCOHOL SYNDROME

55-6 WHY CAN ALCOHOL DRUNK DURING PREGNANCY DAMAGE THE FETUS?

Alcohol is a poisonous substance (teratogen), which, if drunk by the mother during pregnancy crosses the placenta and can interfere with the normal growth and development of the fetus. Both the amount (dosage) and the time (stage of pregnancy) that alcohol is drunk are important.

A past history of heavy alcohol drinking in a woman who does not drink during her pregnancy cannot cause fetal alcohol syndrome.

*** Alcohol may damage the embryo (17-56 days after conception) and the developing fetus (56 days to delivery). The timing and amount of alcohol drunk will determine which organs are damaged and the degree of damage.
55-7 DOES DRINKING ALCOHOL DURING PREGNANCY ALWAYS DAMAGE THE FETUS?

No. Not all women who drink during pregnancy have a child with fetal alcohol syndrome but the risk in South African women who drink heavily during pregnancy is higher than 50 percent.

55-8 HOW MUCH ALCOHOL IS NEEDED TO DAMAGE THE FETUS?

A daily amount of two drinks or more can be harmful. The more alcohol a pregnant woman drinks, the greater is the chance that she will have an infant with fetal alcohol syndrome.

MORE THAN TWO ALCOHOLIC DRINKS A DAY DURING PREGNANCY MAY DAMAGE THE FETUS

One or two drinks a day is regarded as light drinking, three to five drinks a day is moderate drinking while more than five drinks a day is heavy drinking. Therefore, moderate or heavy drinking may damage the fetus. However, any amount of alcohol carries a risk of damaging the fetus. It is not known what mild effects may be caused by light drinking as these are difficult to detect (e.g. a slight reduction in IQ or minor behaviour problems). A woman does not need be an alcoholic for her drinking to damage her fetus.

55-9 WHAT IS BINGE DRINKING?

This is defined as drinking more than five alcoholic drinks at a single occasion. In many South African communities, this is the usual way alcohol is taken and occurs mostly over weekends. The risk of fetal alcohol syndrome is particularly high with binge drinking during pregnancy.

Chronic drinking refers to the pattern of drinking throughout the week. Although chronic drinking is also dangerous to the fetus, the risk of fetal alcohol syndrome is not as high as with binge drinking.

55-10 IS IT BEST NOT TO DRINK ALCOHOL AT ALL DURING PREGNANCY?

Yes. It is best for pregnant women not to drink any alcohol during pregnancy. If they do drink, they should restrict their alcohol intake to no more than one drink a day.

NO AMOUNT OF ALCOHOL IS SAFE DURING PREGNANCY

55-11 HOW MUCH ALCOHOL IS IN ONE DRINK?

One drink is defined as 15 ml of absolute alcohol which is equivalent to a glass of wine (150 ml) or a can of beer (300 ml) or a tot of spirits (25 ml). A quart of beer (the largest container commercially sold and measuring 750 ml) is equivalent to 2.5 drinks and a standard bottle of wine (750 ml) is the same as 5 drinks. An estimate of what a person is drinking must be calculated from the history, taking care to understand what size of container the woman is using.

*** Beer contains 5% alcohol, wine about 10% and spirits approximately 30-40%.

55-12 ARE ALL ALCOHOLIC DRINKS DANGEROUS TO THE FETUS?

Yes. The risk of alcohol damaging the fetus depends on the amount of absolute alcohol taken and NOT the type of drink (e.g. whisky, beer, homebrew and wine). There are no alcoholic drinks which are safe during pregnancy.

ALL FORMS OF ALCOHOL ARE DANGEROUS DURING PREGNANCY

PERINATAL EDUCATION PROGRAMME
55-13  WHEN IS IT MOST DANGEROUS TO DRINK ALCOHOL DURING PREGNANCY?

Drinking alcohol is most dangerous between the four and 10 weeks of gestation (i.e. four to 10 weeks after the last menstrual period), as this may result in damage to the developing organs of the fetus (malformations). The organs most at risk during this time are the brain, heart, kidneys, eye, ear, palate and skeleton. Drinking alcohol during the first trimester may cause congenital malformations of any of these organs.

Therefore, women should stop drinking when they plan to fall pregnant, i.e. before conception.

### DRINKING ALCOHOL IS MOST DANGEROUS DURING THE FIRST TRIMESTER OF PREGNANCY

*** Drinking alcohol between two and eight weeks after conception (i.e. between four and 10 weeks after the start of the last period) may cause malformations in the developing embryo. At this stage some women do not know or are unsure they are pregnant.

55-14  ARE THERE OTHER PERIODS DURING PREGNANCY WHEN ALCOHOL IS DANGEROUS TO THE FETUS?

Yes, alcohol is dangerous throughout pregnancy. Even after 10 weeks of gestation, alcohol can still harm the fetus even though it will not cause congenital malformations. Fetal growth can be affected if alcohol is drunk at any time during pregnancy. If the mother only starts to drink after the first 3 months of pregnancy, the growth of the fetal brain and body can be slowed causing intrauterine growth restriction.

Therefore, there is NO time during pregnancy when it is safe for the mother to drink alcohol.

### WOMEN SHOULD STOP DRINKING ALCOHOL BEFORE THEY CONCEIVE, AND NOT DRINK ALCOHOL DURING PREGNANCY, TO ENSURE THAT THEIR UNBORN INFANTS ARE NOT DAMAGED BY ALCOHOL

55-15  WHAT OTHER FACTORS MAY ALTER THE RISK OF ALCOHOL DAMAGING THE FETUS?

Drinking alcohol affects individuals differently. Some individuals become drunk on small amounts of alcohol while others are unaffected by large volumes. The critical factor that determines the effect of alcohol in a person is the level of alcohol in their blood, the so-called blood alcohol concentration (BAC). An individual is more affected by a high blood alcohol concentration than by a low blood alcohol concentration.

A high maternal blood alcohol concentration also results in a high blood alcohol concentration in the fetus, as alcohol crosses the placenta easily. The higher the fetal blood alcohol concentration, the greater is the risk of damage to the fetus.

### THE MORE ALCOHOL A MOTHER DRINKS, THE GREATER IS THE RISK OF DAMAGE TO HER FETUS

Women who can drink a lot of alcohol before becoming drunk are at a particularly high risk of having an infant with fetal alcohol syndrome as these fetuses are exposed to very high blood alcohol concentrations.
55-16 WHAT FACTORS AFFECT THE BLOOD ALCOHOL CONCENTRATION?

Many factors affect the mother’s blood alcohol concentration and, therefore, the blood alcohol concentration of the fetus:

1. The amount of alcohol drunk.
2. Time taken to drink the alcohol.
4. Food intake at the time of drinking.
5. Smoking and other drug abuse at the same time as drinking alcohol.
7. Maternal malnutrition.

55-17 HOW DOES THE AMOUNT OF ALCOHOL AND THE TIME TAKEN TO DRINK THE ALCOHOL AFFECT THE BLOOD ALCOHOL CONCENTRATION?

There is a direct relationship between the amount of alcohol consumed, the time over which it was taken and the blood alcohol concentration. The greater the amount of alcohol drunk and the shorter the time taken to drink the alcohol, the higher will be the blood alcohol concentration.

Normally, one drink results in a blood alcohol concentration of 20-30 mg% and then the alcohol is completely broken down (metabolised) over a period of two hours. After two drinks, the usual blood alcohol concentration is 60 to 80 mg% and the alcohol is broken down in four hours, and so on.

**DRINKING A LOT OF ALCOHOL FAST RESULTS IN A HIGH BLOOD ALCOHOL CONCENTRATION**

Figure 55-1: The blood alcohol concentration over eight hours after one to four drinks. The greater the number of drinks, the higher the peak blood alcohol concentration and the longer it takes to return to nil.

55-18 HOW DOES MATERNAL WEIGHT AFFECT THE BLOOD ALCOHOL CONCENTRATION?

Each drink results in a higher blood alcohol concentration in women with a low weight than in women who weigh more. Heavier women, therefore, can drink more than light women before they become drunk.
A mother’s weight is related to the amount of water in her body (her total body water). The volume of alcohol drunk passes into all the body water within 20 minutes. A large or heavy person has a large amount of body water and this dilutes the alcohol and reduces the blood alcohol concentration. The reverse is true for a small individual who has less body water to dilute the alcohol, resulting in a higher blood alcohol concentration.

55-19 HOW DOES FOOD INTAKE AFFECT THE BLOOD ALCOHOL CONCENTRATION?

Food, especially carbohydrate foods such as bread, rice or maize products, reduces the absorption of alcohol from the stomach after drinking. This lowers the blood alcohol concentration. Drinking without eating, therefore, results in a higher blood alcohol concentration.

55-20 HOW DOES SMOKING AND OTHER DRUG ABUSE AFFECT THE BLOOD ALCOHOL CONCENTRATION?

When smoking cigarettes and drinking occur together, a higher blood alcohol concentration can be expected than when the same amount of alcohol is taken alone. Similarly, smoking marijuana (dagga) or taking other drugs together with alcohol also raises the blood alcohol concentration. Therefore, the risk of fetal alcohol syndrome is higher if a woman both drinks alcohol and abuses other drugs during pregnancy.

All smoking during pregnancy is strongly contra-indicated as smoking alone may cause poor fetal growth and be a factor in causing such defects as cleft-lip and cleft palate.

55-21 HOW DO GENETIC FACTORS AFFECT THE BLOOD ALCOHOL CONCENTRATION?

Alcohol is broken down in the liver by enzymes. These enzymes occur in two forms. They may either break down alcohol fast or slowly. Fast acting enzymes, which break down alcohol rapidly, result in a lower than expected blood alcohol concentration for the amount of alcohol taken. The opposite is true for the slow acting form of the enzymes which break down alcohol slowly resulting in a higher than expected blood alcohol concentration. The rate at which a mother’s liver breaks down alcohol is determined by whether she has inherited fast or slow acting enzymes from her parents. Individuals with slow acting enzymes are at an increased risk of having an infant with fetal alcohol syndrome.

Two separate enzymes are involved with metabolising alcohol. The first step enzyme breaks alcohol down to acetaldehyde while the second step enzyme break down acetaldehyde to carbon dioxide and water. A rapid first-step enzyme followed by a slow second step enzyme may result in high concentrations of acetaldehyde, which causes nausea in the person who is drinking. Due to these unpleasant side effects, this usually results in smaller amounts of alcohol being drunk by the person with this combination of enzymes. As a result, they usually have a lower blood alcohol concentration. Antabuse, the drug used to stop alcoholics from drinking, uses this mechanism by interfering with the second step enzyme (slowing it) to produce nausea and vomiting in a person who “sneaks” a drink.

55-22 HOW DOES MATERNAL MALNUTRITION AFFECT THE BLOOD ALCOHOL CONCENTRATION?

Maternal undernutrition usually results in an individual with a low body weight. As a result, these women tend to have a higher blood alcohol concentration than a heavier woman who has drunk the same amount. Also, certain trace elements and minerals, such as iron and zinc, may be at lower than normal levels in a malnourished person. Both of these minerals are important in the breakdown of alcohol in the liver, and deficiencies of iron or zinc may, therefore, result in a higher blood alcohol concentration.
A HIGHER BLOOD ALCOHOL CONCENTRATION IS EXPECTED IN WOMEN WHO ARE UNDERWEIGHT, SMOKE, AND DO NOT EAT WHEN THEY DRINK

55-23 DOES MATERNAL AGE AFFECT THE RISK OF FETAL ALCOHOL SYNDROME?

Heavy drinking during pregnancy at any age may cause fetal alcohol syndrome. However, drinkers tend to drink more as they get older and, therefore, the risk of fetal alcohol syndrome increases with maternal age. Maternal nutrition, poverty and general health also tend to become worse over time in heavy drinkers.

This may explain why older mothers may give birth to an infant with fetal alcohol syndrome even if they delivered normal infants when they were young.

RECOGNISING INFANTS WITH FETAL ALCOHOL SYNDROME

55-24 WHAT ARE THE MAJOR FEATURES OF FETAL ALCOHOL SYNDROME?

1. A history of the mother drinking heavily during pregnancy.
2. Characteristic facial features.
3. Slower growth than expected, both before and after delivery.
5. Congenital malformations.

55-25 CAN INFANTS WITH FETAL ALCOHOL SYNDROME BE RECOGNISED AT BIRTH?

Yes. Infants with fetal alcohol syndrome can be recognised at birth as they have typical facial features. The nurse or doctor delivering the infant, or examining the infant after birth, can usually make the diagnosis. Infants with fetal alcohol syndrome are often jittery, irritable and appear anxious after delivery. If the mother drank throughout the pregnancy, this abnormal behaviour could be due to the sudden withdrawal of alcohol to the infant after delivery.

The diagnosis should always be expected if the mother gives a history of heavy drinking during pregnancy. However, when mothers are not suspected of heavy drinking in pregnancy, the diagnosis of fetal alcohol syndrome may be missed.

If the doctor is not sure whether the infant has fetal alcohol syndrome, it may be decided to follow the infant's growth and development before confirming the diagnosis. It is important to be sure of the diagnosis before labelling an infant as having fetal alcohol syndrome.

55-26 AT WHAT AGE IS IT EASIEST TO DIAGNOSE FETAL ALCOHOL SYNDROME?

Although the condition can be recognised at birth, the clinical features of fetal alcohol syndrome often become more obvious when the children are between three and 10 years of age. Therefore, many of these children are only diagnosed later in life.

55-27 WHAT ARE THE CHARACTERISTIC APPEARANCES OF A NEWBORN INFANT WITH FETAL ALCOHOL SYNDROME?

1. Narrow (short) palpebral fissures (distance between the inner and outer corner of the eye).
2. Flattened nasal bridge with epicanthic folds.
3. Short upturned nose.
4. Long, smooth upper lip with no vertical ridge (philtrum) between the nose and the lip.
5. A narrow pink border (vermilion border) of the upper lip (the visible pink part of the upper lip, i.e. the area where a woman puts her lipstick).
7. Deep creases down both sides of the mouth when the infant cries.
8. Flattened cheekbones.

See photographs of children with fetal alcohol syndrome at the end of this unit.

Figure 55-2: The typical facial features of fetal alcohol syndrome.

*** Other features of FAS are ptosis (droopy eye), abnormally shaped teeth, a low hairline over the forehead and nape of the neck (hirsutism), and minor ear abnormalities. They may also have a cleft palate.

55-28 WHY DO INFANTS WITH FETAL ALCOHOL SYNDROME ALL LOOK ALIKE?

Most facial features of fetal alcohol syndrome are due to poor development of the mid-face, giving the typical appearance. The short upturned nose, long smooth upper lip without a philtrum, narrow pink border of the upper lip and small chin are due to underdevelopment of the middle of the face.

The philtrum is the narrow ridge which normal infants have running from their nose to the centre of the upper lip. This is missing in infants with fetal alcohol syndrome.

When infants with fetal alcohol syndrome cry, the pink part of the upper lip becomes stretched and thin. They also have deep creases down both sides of their mouth which are not seen when the infant is not crying. Most of the facial features of fetal alcohol syndrome are more obvious when the infant cries.

55-29 DO THE FACIAL FEATURES OF FETAL ALCOHOL SYNDROME CHANGE WITH AGE?

Yes. The facial features do change with age, and the most useful time to recognise them is between three and 10 years. Before and after this time the typical features are less obvious. After 10 years the facial features appear more normal although the palpebral fissures remain short for life.

With increasing age the flattening of the bridge of the nose fills out and becomes less noticeable while the nose and jaw become longer. If the face of an adolescent or adult with fetal alcohol syndrome is viewed from the side, there is blunting of the tip of the nose, a long upper lip and characteristic jutting shape to the jaw.

Experience is needed to notice these features.

55-30 MAY THE PATTERN OF DRINKING DURING PREGNANCY AFFECT THE FACIAL APPEARANCE OF THE INFANT WITH FETAL ALCOHOL SYNDROME?

Yes. If the mother drinks heavily throughout her pregnancy, but especially between four and 10 weeks of gestation, the characteristic facial appearance will be present. However, if the
mother only drinks after the first 10 weeks of pregnancy, her infant may have a normal face. A confident diagnosis of fetal alcohol syndrome then becomes very difficult.

**IF A WOMAN DRINKS HEAVILY BETWEEN 4 AND 10 WEEKS OF PREGNANCY, HER INFANT WILL BE AT HIGH RISK OF HAVING THE CHARACTERISTIC FACIAL APPEARANCE OF FETAL ALCOHOL SYNDROME**

**55-31 DO INFANTS WITH FETAL ALCOHOL SYNDROME HAVE SMALL EYES?**

No. Their eyes are usually of a normal size. However, their eyes appear small because they have narrow palpebral fissures (the distance between the inner and outer corners of the eye).

**55-32 HOW CAN THE LENGTH OF THE PALPEBRAL FISSURES BE MEASURED?**

The length of the palpebral fissure can be measured with a ruler. This is easier done in older children.

When measuring a young infant’s palpebral fissures, one needs to make sure that the child is awake, relaxed, and not crying. An older child should be asked to maintain a normal facial expression and watch the examiner’s nose. This focuses the child’s attention and prevents the child squeezing the eyes closed.

A ruler should then be placed along the palpebral fissure with the start of the ruler over the inner angle (corner) of the eye (inner canthus). The palpebral fissure length is then measured to the outer angle of the eye (outer canthus). The length of the palpebral fissure can be plotted on a chart giving the palpebral fissure length for age. A palpebral fissure length less than the third percentile (below the normal range) indicates a short palpebral fissure, which is a strong indicator of fetal alcohol syndrome.

Care should be taken not to confuse the inner angle of the eye with an epicanthic fold. The epicanthic fold is a fold of skin at the start of the palpebral fissure often seen in infants. If an epicanthic fold is present, it should be gently lifted away with the examiner’s thumb before measuring the palpebral fissure length.

**GROWTH AND DEVELOPMENT IN INFANTS WITH FETAL ALCOHOL SYNDROME**

**55-33 WHAT IS THE PATTERN OF GROWTH DEFICIENCY IN NEWBORN INFANTS WHO HAVE FETAL ALCOHOL SYNDROME?**

Growth deficiency begins with the fetus and can be measured by serial antenatal ultrasound scans throughout pregnancy. As a result, these infants often have a low birth weight (weigh less than 2500 g at birth). Usually their weight, length and head circumference at birth all fall below the 10th centile for gestational age. They are, therefore, underweight and short for their gestational age (stunted) with small heads. Infants with fetal alcohol syndrome often have a head circumference which is lower than their weight or length on the centile charts (microcephaly).

**INFANTS WITH FETAL ALCOHOL SYNDROME ARE GROWTH RESTRICTED AT BIRTH**
55-34 WHAT ARE THE TYPICAL GROWTH PROBLEMS SEEN IN OLDER CHILDREN WITH FETAL ALCOHOL SYNDROME?

Usually the infant's weight, length and head circumference remain below the 10th percentile. This pattern of slow growth continues into the infant after delivery, even if the child receives a good diet. As a result, mothers of children with fetal alcohol syndrome are often accused of not feeding their children properly.

Both head circumference and length (height) remain less than expected throughout childhood and adolescence, resulting in short adult stature with a small head. The increase in body weight is also slow although girls may become obese at puberty. Boys tend to remain underweight into adulthood.

55-35 WHAT IS THE AFFECT OF ALCOHOL ON BRAIN GROWTH AND DEVELOPMENT?

Head circumference is a good measure of brain size and is often used to assess brain growth. Slow brain growth results in slow head growth. This can be demonstrated in the fetus with serial antenatal ultrasound scans. After delivery, slow brain growth can be recorded by measuring head circumference with a tape and plotting it on a growth chart.

Heavy drinking during pregnancy will slow down brain growth. Depending on the amount and timing, alcohol abuse can result in microcephaly. As well as reducing brain growth, alcohol also damages the brain, especially when alcohol is drunk in the first trimester. Deficient growth and structural damage to the developing brain has serious consequences for the intelligence and behaviour of people with fetal alcohol syndrome.

55-36 ARE ALL PEOPLE WITH FETAL ALCOHOL SYNDROME INTELLECTUALLY DISABLED

Yes. All people with fetal alcohol syndrome are intellectually disabled with an average intelligence (IQ) of 60-70, which is in the mild intellectual disability range (average IQ in normal people is 100). Worldwide, fetal alcohol syndrome is one of the most common preventable causes of intellectual disability.

Infants and children with fetal alcohol syndrome are developmentally delayed. Their motor milestones are often slow and their motor coordination poor. They also have language and behaviour problems.

55-37 WHAT LANGUAGE PROBLEMS ARE COMMON IN CHILDREN WITH FETAL ALCOHOL SYNDROME?

Children with fetal alcohol syndrome have delayed language development. However, once they learn to speak, they are often very talkative although the content is very simple and sentence construction poor.

Hearing loss or deafness, and cleft lip or palate can worsen speech problems. These can also affect the rate of acquiring speech and pronunciation. Hearing loss or deafness may be due to recurrent ear infections, fluid behind the eardrums (chronic serous otitis media) or congenital deafness due to nerve damage.
55-38 WHAT BEHAVIOUR PROBLEMS ARE COMMON IN CHILDREN WITH FETAL ALCOHOL SYNDROME?

Behaviour problems are very common. Infants are often irritable, cry a lot and have feeding problems. This may affect the mother-infant relationship and increases the risk of physical abuse.

Children with fetal alcohol syndrome commonly:

1. Have sleeping problems.
2. Are unable to learn from past mistakes.
3. Have a lack of sense of danger.
4. Have poor concentration (attention deficit disorder).
5. Are hyperactive.

These behavioural abnormalities result in children with fetal alcohol syndrome having:

1. School learning problems. The behaviour problems, especially the poor concentration and hyperactivity associated with intellectual disability, result in school failure and the need for special education.
2. Problems from an early age integrating into society. Stealing, lying, aggression and other abnormal activities are common. These children are often easily influenced by others to take part in anti-social (e.g. alcohol and drug abuse) and criminal activities. They often suffer from anxiety and low self esteem and have difficulty finding employment as adults. Children with fetal alcohol syndrome often become “street children”.

Social development is seriously affected by the behaviour abnormalities, even if these children are placed in stable homes.

*** Poor concentration and hyperactivity in children are also known as attention deficit, hyperactivity disorder (ADHD).

55-39 WHAT LEARNING PROBLEMS ARE COMMON IN CHILDREN WITH FETAL ALCOHOL SYNDROME?

Most children with fetal alcohol syndrome have general learning problems, especially with language, reading, writing, arithmetic and problem solving. Failing at school is common. The poor home environment also adds to the learning and behaviour problems as does attention deficit disorder.

Children with fetal alcohol syndrome have serious life long physical, emotional, intellectual and behaviour problems

55-40 WHAT IS ALCOHOL RELATED NEUROLOGICAL DEFICIT?

Children who are exposed to alcohol only after the first trimester do not suffer the serious effects of alcohol on developing organs. They do not have the typical fetal alcohol face and congenital malformations. However, alcohol later in pregnancy still has harmful effects on brain and body growth resulting in microcephaly and stunting. These children are classified as Alcohol Related Neurological Defect (ARND) and not Fetal Alcohol Syndrome. Because they do not have the typical facial features, they may be difficult to diagnose.
55-41 WHAT CONGENITAL MALFORMATIONS ARE ASSOCIATED WITH FETAL ALCOHOL SYNDROME?

The following malformations are associated with fetal alcohol syndrome:

1. Congenital heart defects. This is the commonest associated malformation. The defect seen most often is ventricular septal defect (VSD) followed by atrial septal defect (ASD).
2. Skeletal abnormalities. These include radio-ulnar synostosis (bony fusion of the two bones seen on X-ray in older children and adults), neural tube defects, vertebral abnormalities, abnormal fingers (4th and 5th), and pectus excavatum (funnel chest).
3. Cleft lip and palate. Usually only a cleft palate is present. This is not common. Therefore examination of the palate with a torch and spatula is necessary if the diagnosis of fetal alcohol syndrome is suspected.

55-42 IS THERE A TEST FOR FETAL ALCOHOL SYNDROME?

Unfortunately there is no specific test for fetal alcohol syndrome. Therefore, a blood test cannot be used to screen children for this disorder. It is a clinical diagnosis based on a careful general examination plus a history of the mother taking alcohol during pregnancy. Great care must be taken in making the correct diagnosis as it has serious implications for the person with fetal alcohol syndrome and the family.

CARE OF CHILDREN WITH FETAL ALCOHOL SYNDROME AND THEIR FAMILIES

55-43 WHAT CARE IS AVAILABLE FOR PEOPLE WITH FETAL ALCOHOL SYNDROME?

People with fetal alcohol syndrome, as with all people with congenital disability, should be offered the “best possible patient care” available. This includes care of their medical problems and meeting their special needs:

1. It is important to make and confirm the diagnosis of fetal alcohol syndrome as early as possible. This allows for early genetic counselling to inform parents about the disorder and available treatment, and helps them come to terms with the many problems and to emotionally bond with their child. It also allows for an early start to treatment and intervention programmes. This will ensure the best long-term outcome for the person’s health, development and intellectual ability.
2. Newborns should be kept warm and fed early to prevent hypoglycaemia and hypothermia caused by their growth restriction.
3. Ear infections should be diagnosed early and treated correctly with antibiotics.
4. Behaviour problems should be managed. This is a specialised area of treatment and people with fetal alcohol syndrome should be referred to special units.
5. Children with congenital heart defects may need to be treated for heart failure.
6. Surgical repair for congenital heart defects may be needed. Infants and children, suspected of having congenital heart defects, should be sent for cardiac assessment.
7. Other congenital malformations such as cleft lip or palate will need surgical correction.

PEOPLE WITH FETAL ALCOHOL SYNDROME, LIKE ALL PEOPLE WITH DISABILITY, SHOULD GET THE BEST POSSIBLE CARE AVAILABLE FOR THEM
55-44 HOW SHOULD DEVELOPMENTAL AND BEHAVIOURAL PROBLEMS BE MANAGED?

They should be offered neurodevelopmental therapy and community based rehabilitation. Infants and children with fetal alcohol syndrome develop slowly, are intellectually disabled and have behaviour problems. Their successful integration into society, including schooling and finding employment, is difficult and will be greatly improved by early diagnosis and intervention. This includes:

1. Physiotherapy to assist those infants with slow motor milestones achieve their motor milestones faster.
2. Hearing assessment (audiology) and speech therapy. Infants and children with fetal alcohol syndrome have delayed speech development and this may be worsened by hearing loss from recurrent ear infections or congenital auditory (hearing) nerve damage. Hearing must be checked if deafness is suspected. Speech therapy helps them to develop better speech faster.
3. Occupational therapy. Fine motor co-ordination and personal and social development can be improved by an occupational therapist.

Neurodevelopmental therapy in all its forms is available in major centres. However, in less resourced rural and urban regions, this may only be available in the form of community based rehabilitation. In South Africa, community based rehabilitation for infants and children with disability can be assisted by the use of a locally produced stimulation program called START.

*** Information on START can be obtained from: Sunshine Centre, P O Box 411567, Craighall, 2024. Telephone 011 642 2005.

55-45 SHOULD CHILDREN WITH FETAL ALCOHOL SYNDROME GO TO SCHOOL?

All children with fetal alcohol syndrome should have the opportunity of going to school, despite the fact that they will have school learning problems. In South Africa at present, the Department of Education’s policy is “inclusive” education for children with mild intellectual disability. The aim of the policy is to allow disabled children to attend normal schools where they will be integrated into the education programme to the greatest extent possible, but will also have available the specialised attention they need. Because of their behaviour problems it may be necessary for the caregivers to work together with the school on the child’s educational management. The other option is for these children to go to a school for the intellectually disabled. There are a few of these special schools in South Africa.

55-46 SHOULD INFANTS WITH FETAL ALCOHOL SYNDROME BE BREASTFED?

Yes. However, alcohol crosses into the breast milk in small amounts. Therefore, the mother should be encouraged not to drink alcohol during the period that she is breast feeding. Emotional bonding and infant nutrition can be improved with breast feeding, especially when the home economic conditions are poor.

55-47 WHAT GENETIC COUNSELLING IS NEEDED BY PARENTS WHO HAVE A CHILD WITH FETAL ALCOHOL SYNDROME?

Genetic counselling is a major part of the care of people with fetal alcohol syndrome and their family, especially the parents. The parents need to be educated and informed about:

1. The diagnosis.
2. The cause of fetal alcohol syndrome.
3. The clinical features, complications and prognosis of fetal alcohol syndrome, and the treatment available.
4. The risk for parents with a child with fetal alcohol syndrome having another child with fetal alcohol syndrome in future pregnancies. The risk can be eliminated if the mother does not drink alcohol during all future pregnancies. If possible, she should stop drinking alcohol completely.

PERINATAL EDUCATION PROGRAMME
The parents, family and child with fetal alcohol syndrome need to be offered on-going psychosocial support as with all individuals who have a congenital disability. They suffer lifelong problems which require lifelong care including support. The burden of the disorder is experienced not only by the affected person, but also the family, especially parents, brothers and sisters. Support, help, reassurance and care in these circumstances may be obtained from:

1. Doctors, nurses (especially genetic trained nursing staff), genetic counsellors and neurodevelopmental therapists.
2. Teachers in special schools for the intellectually disabled.
4. The Foundation for Alcohol Related Research (FARR). This non-governmental organisation plays a role in South Africa in advocacy, patient and parent support, and educating the public and medical and para-medical professions (Contact details: FARR, c/o Division of Human Genetics, National Health Laboratory Service, P O Box 1038, Johannesburg, 2000).

55-48 CAN FETAL ALCOHOL SYNDROME BE PREVENTED?

The answer is theoretically yes if the woman does not drink any alcohol in future pregnancies. The reality may be different. It is very difficult to prevent alcohol consumption in all women who may fall pregnant. It is also difficult to persuade heavy drinkers not to drink. However, there has been some success in reducing or stopping drinking in women who have previously had a child with fetal alcohol syndrome. The alternative is to try and persuade women, who are at risk, to delay becoming pregnant by using contraception until such time as they can reduce or stop drinking alcohol.

In the long term, educating the whole community about the dangers of drinking may be the best approach to preventing fetal alcohol syndrome. FARR is currently undertaking research on how to achieve this in South Africa.

*** Many alcoholic drinks have a health warning on the label but it is uncertain whether this reduces the risk of fetal alcohol syndrome.

EVERY EFFORT MUST BE MADE TO STOP WOMEN DRINKING ALCOHOL DURING PREGNANCY TO PREVENT FETAL ALCOHOL SYNDROME

55-49 HOW CAN YOU IDENTIFY WOMEN AT RISK OF DELIVERING AN INFANT WITH FETAL ALCOHOL SYNDROME?

The following factors are associated with women at high risk:

1. A previous child with fetal alcohol syndrome. This is the most important risk factor.
2. Women who admit to heavy drinking.
3. Women with a husband or partner who drinks heavily.
4. Women from a community or household where alcohol is abused.
5. A high suspicion that the woman drinks heavily.

All women must be asked about these risk factors when they book for antenatal care. Mothers should also be asked about these risk factors if their child is suspected of having fetal alcohol syndrome. It is important not to be judgmental when taking a history of alcohol intake. The amount and frequency of alcohol drunk should be established.

55-50 HOW SHOULD THE WOMAN AT RISK OF DELIVERING AN INFANT WITH FETAL ALCOHOL SYNDROME BE MANAGED?

1. She must be informed of the risk to her unborn infant.
2. She should be provided with the information needed to make an informed decision about her drinking, i.e. counselled.

PERINATAL EDUCATION PROGRAMME
3. She should be referred to the appropriate facilities or resources in the community where she can obtain help and support, e.g. social services, churches, women’s groups, schools, employers and community workers.

4. Women who are trying to stop abusing alcohol need the support of the whole community.

**PREVENTING FETAL ALCOHOL SYNDROME IS FIRSTLY A COMMUNITY ISSUE, BUT ALSO A NATIONAL CONCERN**

**CASE STUDIES**

**CASE 1.**

A mother of two normal children drinks heavily throughout her pregnancy. She tells her friends that fetal alcohol syndrome is rare and is inherited. Because her children are healthy she believes that there is no danger to her fetus.

1. **How common is fetal alcohol syndrome?**

   Although it is rare in industrialised countries (one in 1000 births) it is common in South Africa, especially in poor communities where more than 50 per 1000 infants may be affected.

2. **Is fetal alcohol syndrome inherited?**

   No. However, the rate at which alcohol is broken down in the body is inherited. Therefore, women who inherit a slow rate of breaking down alcohol are at an increased risk of a damaged fetus as they have higher blood concentrations of alcohol if they drink.

3. **Do two normal children indicate that she has no risk of damaging this fetus with alcohol?**

   No. Many women who drink a lot of alcohol tend to drink more as they get older. Therefore their later children are at a particularly high risk of fetal alcohol syndrome.

4. **Would the fetus be safe if the mother only drank in the second half of pregnancy?**

   Alcohol is more dangerous in the first 10 weeks of pregnancy when the fetal organs are still forming. Heavy drinking during early pregnancy may, therefore, cause congenital malformations. However, drinking in later pregnancy may still interfere with the growth and development of the fetus. Some infants exposed to alcohol only late in pregnancy appear normal at delivery but still have brain damage (alcohol related neurological deficit). Therefore alcohol is dangerous at any time during pregnancy.

5. **Is it safe for a mother who drinks heavily to breast feed her infant?**

   As small amounts of alcohol cross into the breast milk, it is best if a mother does not drink alcohol during the weeks and months that she is breast feeding.
CASE 2.

A young, thin woman who is pregnant with her first child goes to a party one Saturday evening with her boyfriend and gets very drunk. They both drink five 300 ml cans of beers in less than an hour. She also smokes a few cigarettes but has very little to eat.

1. **Is it dangerous if she only drinks heavily once during her pregnancy?**

Taking a lot of alcohol even once is dangerous to a fetus. Binge drinking like this can severely damage a fetus, especially in the first trimester.

2. **How much alcohol is safe for a pregnant woman to drink?**

Any amount of alcohol carries a risk of fetal damage, but especially with more than two drinks a day. It is best to drink no alcohol during pregnancy.

3. **Does it matter how fast the alcohol is drunk?**

The greater the amount of alcohol and the faster it is drunk, the higher will be the blood alcohol concentration. The higher the blood alcohol concentration, the greater the risk of damage to the fetus.

4. **How can one determine how many drinks there are in five 300 ml cans of beer?**

One drink is equal to one 300 ml can of beer, one 150 ml glass of wine or a 25 ml tot of spirits. Five beers are equivalent to five drinks. This is a large amount of alcohol.

5. **Are some types of alcohol less dangerous to the fetus than others?**

No. The risk to the fetus depends on the amount of alcohol not on the type of drink, e.g. beer, wine or spirits.

6. **What other factors may have influenced her blood alcohol concentration?**

She is thin (and probably does not weigh very much), smokes and has little to eat. These factors will all result in a relatively high blood alcohol concentration.

CASE 3.

A midwife notices that a newborn infant has a strange facial appearance. The infant weighs less than 2500 g at birth and the head appears particularly small. The mother admits to drinking heavily throughout her pregnancy.

1. **What is the typical appearance of the face in infants with fetal alcohol syndrome?**

They have short palpebral fissures and a long smooth upper lip without a philtrum. There are also deep creases down both sides of the mouth and not much pink upper lip to be seen, especially when the infant cries. Most of these, and other facial features of fetal alcohol syndrome, are due to poor growth of the central part of the face.

2. **What is the size at birth of most infants born with fetal alcohol syndrome?**

Most have a low birth weight (less than 2500 g). Their weight, length and especially head circumference measurements are less than expected for their gestational age (less than the 10th centile). The small head indicates that the infant’s brain has been growing slowly during pregnancy.
3. How may the pattern of drinking during pregnancy affect the appearance of the infant?

The facial abnormalities are most marked if the mother drinks heavily during the first months of pregnancy (4 to 10 weeks after the last menstrual period).

4. At what age is the appearance of fetal alcohol syndrome most easy to recognise?

Although these infants can be recognised at birth, their abnormal appearance is most marked between three and 10 years of age. Most infants with fetal alcohol syndrome look similar, and with experience can be recognised.

5. What congenital malformations can be caused by heavy drinking during pregnancy?

Excessive alcohol intake during pregnancy not only damages the growth and development of the fetus but can also cause congenital malformations, especially of the heart (ventricular and atrial septal defects), skeleton and palate.

6. Is there a blood or other test that can prove the diagnosis of fetal alcohol syndrome?

No. The diagnosis is based on the mother's history of drinking alcohol during pregnancy and the pattern of clinical signs in the infant. There is no specific test for fetal alcohol syndrome.

CASE 4.

A 10 year old child with fetal alcohol syndrome is having major schooling problems. The teacher complains of bad behaviour. The child is not able to keep up with the other normal children in the class and does not pay attention.

1. Why do children with fetal alcohol syndrome often fail at school?

All children with fetal alcohol syndrome have reduced intelligence and learning difficulties and, therefore, failing at school is common. The main problem is brain damage caused by exposure to alcohol during pregnancy. In addition, there are often many social problems at home.

2. What learning problems are common?

Children with fetal alcohol syndrome have particular problems with language, reading, writing, arithmetic and problem solving. It is, therefore, not surprising that they often fail at school.

3. What is the average intelligence of children with fetal alcohol syndrome?

Most have a low IQ (intelligence quotient) of 60 to 70. This places them in the range of mildly intellectually disabled. Fetal alcohol syndrome is one of the most common preventable causes of intellectual disability.

4. What language difficulties occur in these children?

They have delayed language development, i.e. they learn to talk later than normal. However, once they are able to speak, they tend to be very talkative, using simple poorly constructed sentences.
5. Are behaviour problems common in fetal alcohol syndrome?

Yes, behaviour problems are common. Young infants with fetal alcohol syndrome are irritable and cry a lot which often affects the mother-infant relationship and can result in child abuse. Older children are hyperactive with poor concentration (attention deficit). Anti-social behaviour with lying, stealing and aggression may lead to criminal acts.

6. Should a child with fetal alcohol syndrome go to a normal school?

All children with fetal alcohol syndrome should go to school and, if possible, attend a normal school. As most of these children have mild intellectual disability they will need extra help. Some more seriously impaired children may need to go to a special school, if it is available.

CASE 5.

Parents of a very difficult child with fetal alcohol syndrome visit a local clinic for help and advice. They want to know what can be done to help them care for the child. They also ask about the risks of having another child with fetal alcohol syndrome as they still drink heavily.

1. What care is available for children with fetal alcohol syndrome?

Parents of a child with fetal alcohol syndrome need a lot of help and psychosocial support. Neurodevelopmental therapy is important and includes physiotherapy, hearing assessment and speech therapy, and occupational therapy. Doctors, nurses, teachers and social workers all have a role to play. Comprehensive care can be offered in special units in most larger centres in South Africa. Hospital and community based services to provide neurodevelopmental therapy and stimulation programme are becoming available in other regions. Local support groups can be of great help.

2. Do children with fetal alcohol syndrome need special medical treatment?

Ear infections are common and need to be diagnosed and treated early. Congenital malformations such as heart defects and cleft palate will need correct treatment.

3. What factors identify a women at risk of having another child with fetal alcohol syndrome?

The most important risk factor is a previous child with fetal alcohol syndrome. However, a history or suspicion of heavy drinking from the woman, her partner or the local community is also associated with an increased risk. This should always form part of the history taken at an antenatal clinic.

4. Can fetal alcohol syndrome be prevented?

Only by not drinking alcohol throughout pregnancy. This is not easy for a woman who drinks heavily. Perhaps her best option, if she cannot stop drinking, is to delay having further pregnancies, by using contraception.

5. How should this woman be helped?

She must be advised about the risk of damage to her unborn child if she drinks during pregnancy, and be given the information she needs to make an informed decision about her drinking. Both parents should be referred to a local resource in the community such as a social worker, church group or community worker. People can stop drinking but they need the help and support of the whole community if they are to succeed.
PHOTOGRAPHS OF CHILDREN WITH FETAL ALCOHOL SYNDROME

Picture 55-A: Typical facial appearance of an infant with fetal alcohol syndrome.

Picture 55-B: Four children with fetal alcohol syndrome in a single family.
OBJECTIVES

When you have completed this unit you should be able to:

1. Define a neural tube defect.
2. List the three types of neural tube defect.
4. Explain the causes of neural tube defects.
5. Describe the clinical features of neural tube defects.
7. Counsel parents of children with neural tube defects.
8. Reduce the risk of neural tube defects.

COPYRIGHT

All rights reserved. No part of this Perinatal Education Programme may be altered in any way, nor may copies of the complete Programme be made, without the written permission of the editorial board of the Perinatal Education Trust. To facilitate the improvement of perinatal care, however, parts of the Programme may be reproduced for teaching purposes provided due acknowledgement is given and the material is not sold for financial profit. While the advice and information in the Programme are believed to be accurate, the editorial board cannot accept responsibility or liability for any errors or omissions that may have been made.

ISBN 0 7992 2254 2
56-1 WHAT ARE NEURAL TUBE DEFECTS?

Neural tube defects (NTDs) are malformations of the neural tube, caused by failure of the neural tube to close at the end of the fourth week after conception. Neural tube defects include the following three conditions:

1. Anencephaly.
2. Encephalocele.
3. Spina bifida.

Neural tube defects are typical examples of a **multifactorial defect** which results from an interaction between genetic factors (usually a number of inherited genes) and an environmental factor (probably viral, dietary, toxic or radiation). Multifactorial defects, such as neural tube defects, occur in both males and females.

56-2 WHAT IS THE NEURAL TUBE?

At 22 days after conception, the embryo is a flat, pear shaped plate made up of three layers of cells. By a process of folding in the midline, the top layer of cells forms a tube within the middle layer of the plate. This tube, which runs from top to bottom of the developing embryo, is the neural tube.

Figure 56-1: The three layers of the embryonic plate showing the folding to form the neural tube.
56-3 WHAT DEVELOPS FROM THE NEURAL TUBE?

The neural tube is the structure from which the skull, brain, spinal cord and nerves will develop, as well as the spinal column (made up of vertebrae). If the neural tube fails to close at the head end, the defect results in anencephaly or an encephalocele. If it fails to close lower down along the spine, the result is spina bifida.

ANENCEPHALY, ENCEPHALOCELE AND SPINA BIFIDA ARE THE THREE TYPES OF NEURAL TUBE DEFECT

56-4 WHAT IS ANENCEPHALY?

Anencephaly (no brain) is the most serious of all neural tube defects and always results in stillbirth or early neonatal death. The top (vault) of the skull is absent, exposing the brain, which is malformed. The cerebral hemispheres do not develop with anencephaly.

Anencephaly is called an open neural tube defect because brain (neural tissue) is exposed.

An illustration of anencephaly is shown at the end of this unit.

56-5 WHAT IS AN ENCEPHALOCELE?

An encephalocele is a failure of closure in the midline of the skull anywhere from a position between the eyes (frontal area) to the back of the skull (occipital area). With an encephalocele the brain coverings (the meninges), with or without brain tissue, protrude through the skull defect into a membranous sac which is covered by skin. The most common site of an encephalocele is in the occipital area. Frontal encephaloceles are also seen.

ENCEPHALOCELES ARE CALLED CLOSED NEURAL TUBE DEFECTS BECAUSE NEURAL TISSUE IS NOT EXPOSED AS THE DEFECT IS COVERED BY SKIN.

An illustration of an encephalocele is shown at the end of this unit.

56-6 WHAT IS SPINA BIFIDA?

Spina bifida (split spine) is an opening in the spinal column due to failure of closure of the bony vertebral arches. Spina bifida may occur anywhere down the spinal column. There are three forms of spina bifida:

1. Meningomyelocele. This is the most severe form of spina bifida.
2. Meningocele. This is a less severe than meningomyelocele.
3. Spina bifida occulta. This is the least severe form as it only involves the bony spine.

Spina bifida may be either open or closed, depending on the type.
*** Meningomyelocele (or myelomeningocele) is also referred to as spina bifida cystica while meningocoele is also called spina bifida aperta. Cystica is Latin for cyst and aperta means an opening.

56-7 WHAT IS A MENINGOMYELOCOELE?

A meningomyelocele is an opening anywhere along the spinal column, due to failure of one or more vertebral arches to close. Neural tissue (spinal cord and nerves) and the coverings of the spinal cord (the meninges) bulge through the opening. The skin over this defect does not close, but the defect may be covered by a thin membrane which tears easily. The neural tissue that bulges through the bony defect is usually damaged, resulting in nerve abnormalities below the level of the defect.

Meningomyeloceles are open neural tube defects because neural tissue (spinal cord and nerves) is exposed and not covered by skin.

Figure 56-2: A cross section of the spinal column showing a meningomyelocele with both the spinal cord and meninges protruding through a defect in the vertebral arches.

56-8 WHAT IS A MENINGOCOELE?

A meningocoele is an opening anywhere along the spinal column, due to failure of closure of one or more vertebral arches. Only the coverings of the spinal cord (the meninges) protrude through the defect, forming a sac which is filled with cerebrospinal fluid (CSF). The spinal cord and nerves are normal and do not bulge through the opening. There is no associated spinal cord or nerve damage. The meningocoele usually is covered on the outside by skin.

A meningocoele is a closed neural tube defect when it is covered by skin.

Figure 56-3: A cross section of the spinal column showing a meningocoele with only the meninges protruding through a defect in the vertebral arches.
Vertebral body

Normal spinal cord

Meningocele covered with skin

Meningeal sac filled with cerebrospinal fluid only
**56-9 WHAT IS SPINA BIFIDA OCCULTA?**

Spina bifida occulta is a defect of the spinal column, due to failure of one or more vertebral arches to close. This usually occurs in the lumbar and sacral regions of the spine (lower back). Unlike a meningomyelocele or meningocele, the spinal cord and meninges are normal and do not protrude through the defect. The defect may be covered by an overlying abnormality such as a midline patch of hair, a lipoma or a dimple. Neurological abnormality is usually not associated with spina bifida occulta although spina bifida occulta may present later in life with back problems. The diagnosis of spina bifida occulta can be confirmed on X-ray which shows the defect in the spinal column.

Spina bifida occulta is a closed neural tube defect.

*** Occulta is a Latin word that means hidden or secret.

Figure 56-4: A cross section of the spinal column showing spina bifida occulta with neither the spinal cord nor the meninges protruding through a defect in the vertebral arches.

---

**56-10 HOW COMMON ARE NEURAL TUBE DEFECTS?**

Neural tube defects occur throughout the world. Their birth prevalence (number of infants with neural tube defects per 1000 live births) varies according to the area (geographic location), the ethnicity and the socio-economic status of the population. In industrialised countries the birth prevalence of neural tube defects has decreased significantly over the last 40 to 50 years, and is now about 1/1000 live births. Of these infants about 40% have anencephaly, 50% spina bifida and 10% encephaloceles.

In urban areas of South Africa (Cape Town, Johannesburg and Pretoria), the birth prevalence in the African population is about 1/1000 live births. In contrast, the birth prevalence has been recorded as 6.1/1000 in rural areas of the Eastern Cape Province and 3.6/1000 in rural Limpopo Province. The reason for the difference in birth prevalence between urban and rural populations is not known.

The prevalence (number of infants with neural tube defects per 1000 in a population) of neural tube defects in South Africa is small as most infants born with these defects die young. In rural Limpopo more than 90% of infants born with anencephaly, encephalocoele or meningomyelocele die before the age of two years.
IN AFRICAN POPULATIONS IN SOUTH AFRICA, THE BIRTH PREVALENCE OF NEURAL TUBE DEFECTS IN URBAN AREAS IS ABOUT 1/1000 LIVE BIRTHS WHILE IN RURAL AREAS IT IS ABOUT 4/1000 LIVE BIRTHS

*** The birth prevalence of neural tube defects in industrialised countries has decreased greatly over the last 40 years as the socio-economic situation has improved and prevention strategies have been put in place. As an example, in people of Celtic origin living in Ireland, the birth prevalence of neural tube defects used to be above 6/1000 live births but is now less than 1/1000 live births.

56-11 WHAT CAUSES NEURAL TUBE DEFECTS?

The development of the neural tube, including its closure, is under the control of several genes working together with environmental factors. Most neural tube defects are, therefore, caused by multifactorial inheritance, i.e. they result from an interaction between genetic and environmental factors.

MOST NEURAL TUBE DEFECTS ARE DUE TO MULTIFACTORIAL INHERITANCE

Folic acid is one of the important environmental factors essential for closure of the neural tube.

FOLIC ACID IS AN IMPORTANT ENVIRONMENTAL FACTOR IN THE CAUSE OF NEURAL TUBE DEFECTS

56-12 WHAT ARE THE OTHER CAUSES OF NEURAL TUBE DEFECTS.

Neural tube defects can also be caused by chromosomal abnormalities, single gene defects and teratogens including alcohol and sodium valproate (Epilim or Convulex). Sodium valproate is used to treat epilepsy. Some of these drugs may work against the beneficial effect of folic acid.

56-13 WHAT ARE THE CLINICAL FEATURES OF NEURAL TUBE DEFECTS?

The clinical presentation of neural tube defects depends on the type of defect, whether it is open or closed, its position and size. The different presentations vary greatly, from no obvious clinical features in spina bifida occulta to a gross abnormality in anencephaly.

56-14 WHAT ARE THE CLINICAL FEATURES OF ANENCEPHALY?

Infants with anencephaly are often born preterm and may be stillborn. If they are live born they seldom live longer than 24 hours. The infants are born with the top of their skull missing and brain exposed. The eyes appear to bulge. General examination of the rest of the infant is usually normal but may reveal other abnormalities.

*** At post mortem examination 40% of anencephalics have abnormal internal organs.

56-15 WHAT ARE THE CLINICAL FEATURES OF AN ENCEPHALOCELE?

An encephalocele develops because of failure of complete closure of the skull. The infant presents at birth with a midline mass anywhere from between the eyes to the back of the skull (occiput). The most common site for an encephalocele is over the occiput. The clinical presentation will depend on the size and site and whether the encephalocele contains neural tissue (brain matter) or not. Encephaloceles that only contain meninges and no neural tissue usually have problems only related to the defect in the skull. However, if the encephalocele contains brain tissue, this can be damaged or be associated with severe brain abnormalities. The resulting neurological abnormalities will depend on the size and site of the encephalocele. In severe cases, most of the brain may be in the encephalocele.
Associated neurological abnormalities include:

1. Intellectual disability.
2. Microcephaly.
3. Cerebral palsy.
4. Visual disability (blindness)
5. Epilepsy.

Depending on the size and site of the encephalocele, early death, even with treatment, is a common outcome in many of these infants.

56-16 WHAT ARE THE CLINICAL FEATURES OF A MENINGOMYELOCOELE?

A meningomyelocele presents at birth with a mass anywhere along the spine, but usually in the thoracic, lumbar or sacral regions. The mass may or may not be covered by a thin membrane, but neural tissue (spinal cord and nerves) is usually visible. The associated clinical features depend on the site and size of the defect.

As a meningomyelocele contains neural tissue which is usually damaged, the body and limbs of the affected infant are paralysed below the level of the defect. The effect is similar to traumatic cutting of the spinal cord. The associated clinical features include:

1. Flaccid paralysis (floppiness, weakness and absent reflexes) of the legs.
2. No feeling (touch or pain) below the level of the defect.
3. Kyphosis. A forward bend in the spine. With large meningomyelocele this may also be associated with a lateral bend (scoliosis).
4. Incontinence of bladder.
5. Incontinence of bowel.
6. Clubfeet.
7. Hydrocephalus (80% of cases). Hydrocephalus (excessive cerebrospinal fluid in the ventricles of the brain) often presents in utero but may only present in the first weeks after delivery. Early diagnosis of hydrocephalus is important to obtain the best results from surgery.

*** The hydrocephalus is caused by a malformation at the base of the brain, called an Arnold–Chiari malformation, where the cerebellum bulges through the opening at the base of the skull. This blocks the normal flow of cerebrospinal fluid.

56-17 WHAT ARE THE COMPLICATIONS OF A MENINGOMYELOCOELE?

Complications of meningomyelocele may present early or repeatedly. These include:

1. Meningitis. Infection can easily and rapidly enter the nervous system through the open meningomyelocele. Therefore, the meningomyelocele should be carefully and aseptically covered at birth and then closed, as soon as possible, by surgery. Sometime the covering membrane may leak or rupture (tear) during delivery.
2. Raised intracranial pressure due to hydrocephalus. Early signs of increased intracranial pressure are a bulging anterior fontanelle, irritability, vomiting, and a high-pitched cry.
3. Intellectual disability. The hydrocephalus, which may develop before or after delivery, can result in intellectual disability. Epilepsy from the hydrocephalus may also result.
4. Urinary tract infections. The bladder incontinence can result in urinary tract infections in both males and females.
5. Bed sores. These result from the lack of feeling (sensation) and movement in the body below the meningomyelocele.

In low resource countries, infant and early childhood death is a common outcome of meningomyeloceles.
56-18 WHAT ARE THE CLINICAL FEATURES OF A MENINGOCOELE?

A meningocoele presents at birth with a skin covered mass in the midline anywhere along the spine. As the spinal cord and nerves are not involved there usually are no neurological abnormalities in the trunk, limbs, bladder and bowels. However, hydrocephalus is present in 20% of infants with meningocoeles.

HYDROCEPHALUS DEVELOPS IN 80% OF INFANTS WITH MENINGOMYELOCOELES AND IN 20% OF INFANTS WITH MENINGOCOELES

56-19 WHAT ARE THE CLINICAL FEATURES OF SPINA BIFIDA OCCULTA?

Most people with a spina bifida occulta do not know that they have a neural tube defect, i.e. it often remains hidden for life, therefore, the use of the word ‘occulta’ (hidden). They usually have no signs or symptoms. Occasionally, spina bifida occulta is diagnosed on an X-ray which is taken for some other reason. In some infants the presence of the bony defect in the vertebral arches is suggested by an overlying midline abnormality, usually a hairy patch.

*** Very occasionally a child may develop neurological complications of spina bifida occulta, especially during periods of rapid growth, presenting with urinary incontinence, neurological signs of nerve damage in a limb or clawing of the toes due to weakness of muscles in the feet.

CARING FOR INFANTS AND CHILDREN WITH NEURAL TUBE DEFECTS

56-20 WHAT CARE IS AVAILABLE FOR INFANTS WITH NEURAL TUBE DEFECTS?

The care required will depend on the type of neural tube defect, its site and size, and the available health facilities. In all patients the best possible patient care available must be given. This will include:

1. Diagnosis:

Because of the obvious physical features of most forms of neural tube defects the diagnosis is made at birth or shortly thereafter. The exception is spina bifida occulta which is usually not clinically obvious at birth.

2. Treatment:

Infants with anencephaly do not survive and are given palliative (hospice) care with warmth, feeds if hungry and support for the parents.

a. Medical treatment:

Medical treatment may be needed for the complications of encephalocele, and meningomyelocele. These include:

(i) Antibiotics for meningitis if it develops in infants with a meningomyelocele.
(ii) Antibiotics for urinary tract infections in meningomyelocele.
(iii) Recurrent catheterisation for urinary incontinence in meningomyelocele.
(iv) Anticonvulsants for epilepsy in encephalocele.

b. Surgical treatment:

(i) Infants with encephalocele, meningomyelocele and meningocoele should be referred to a neurosurgical unit for assessment. Meningocoeles should be simply covered with a piece of sterile gauze after delivery to reduce the risk of infection before surgery.
(ii) In encephaloceles, meningomyeloceles and meningoceles, surgery is used to close the defect and remove the mass caused by the protruding brain, spinal cord or meninges. Care is taken not to damage the spinal cord and nerves in the repair of meningoceles nor cause further damage to the brain in encephaloceles that contain neural tissue. These infants with neural tube defects need to be referred to a tertiary care hospital for surgical assessment as soon as possible after birth.

(iii) In meningomyeloceles and meningoceles, surgery to insert a ventriculo-peritoneal (VP) shunt to treat hydrocephalus may be required. A shunt is a tube that drains the fluid from the ventricles of the brain into the peritoneum. If the affected infant does not have hydrocephalus at birth, it may develop after the spinal defect is repaired. Therefore, regular careful head circumference measurements must be taken and plotted on a centile chart to help make the diagnosis of hydrocephalus as early as possible (head circumference measurements weekly for the first six weeks and then monthly to one year of age). If ultrasound facilities are available, serial head ultrasound examination can be used to assist in the diagnosis.

c. Neurodevelopmental therapy:

(i) Neurodevelopmental therapy includes physiotherapy, hearing assessment (audiology) speech therapy and occupational therapy may be needed. All these forms of neurodevelopmental therapy are available in major centres. However, in both rural and urban areas with fewer resources, hospitals may only have a physiotherapist or an occupational therapist. Some may also have a community based rehabilitation programme.

(ii) In South Africa, rehabilitation for infants and children with disabilities can be assisted by the use of a locally produced stimulation programme called START (Strive Towards Achieving Results Together). This was designed to use affordable, locally available, materials.

*** Information on START can be obtained from, Sunshine Centre, P. O. Box 411567, Craighall, 2024. Telephone 011 642 2005.

3. Genetic counselling and psychosocial support:

This is an important part of the care of people with neural tube defects and their families.

GENETIC COUNSELLING FOR NEURAL TUBE DEFECTS

56-21 WHAT GENETIC COUNSELLING IS NEEDED BY PARENTS WHO HAVE A CHILD WITH A NEURAL TUBE DEFECT?

Genetic counselling is a very important part of the care of people with neural tube defects and their family, especially the parents and siblings. The parents need to be educated and informed about:

1. The diagnosis.
2. The cause of neural tube defects. They need to know that neural tube defects are usually caused by multifactorial inheritance, but occasionally are the result of other causes. It is important to rule out these other causes if possible.
3. The clinical features, complications and prognosis of the particular neural tube defect their child has, and what treatment is available.
4. The increased risk for parents of a child with a neural tube defect of having another child with a neural tube defect in future pregnancies. They need to know their options for reducing their risk of having another affected child through primary prevention, genetic screening, prenatal diagnosis and genetic counselling.
The parents, family and child with a neural tube defect need to be offered on-going psychosocial support, as do all individuals who have a congenital disability. They have problems that require lifelong care. The burden of the disorder and the care is experienced not only by the affected person, but also the family, especially parents, brothers and sisters.

See Unit 52 of the Perinatal Education Programme for the care, prevention and counselling needed for individuals with neural tube defects and their family.

**56-22 WHERE CAN PARENTS WHO HAVE A CHILD WITH A NEURAL TUBE DEFECT GET SUPPORT?**

Support, help and reassurance may be obtained from:

1. Doctors, nurses (especially genetic-trained nursing staff), genetic counsellors and neurodevelopmental therapists.
2. Social workers.
4. Parent Support Group

*** The Southern African Inherited Disorders Association (SAIDA) can be contacted at the Division of Human Genetics, National Health Laboratory Service, P. O. Box 1038, Johannesburg, 2000, South Africa. Telephone and fax 011 4899213.

**56-23 CAN NEURAL TUBE DEFECTS BE PREVENTED?**

Yes. There are two approaches for the prevention of neural tube defects. These are:

1. Primary prevention: This aims to ensure the conception of infants without neural tube defects. The pre-conception approach is the preferred method of prevention. It is based on the knowledge, confirmed in Europe in the early 1990s, that if a woman takes periconceptional folic acid supplements, she can reduce her risk of having an infant with a neural tube defect by 50 percent. It was also confirmed, that if a woman had previously had an infant with a neural tube defect, her increased risk of having another child with a neural tube defect could be decreased by 70 percent.

*** Research done recently in China showed that periconceptional folic acid supplementation taken by women in the poorer, more rural, northern region where the birth prevalence of neural tube defects is greater than 6/1000 live births, reduced the birth prevalence by 80 percent. In the southern, wealthier and more urban part of China, where the birth prevalence of neural tube defects is about 1/1000, live births periconceptional folic acid reduced the birth prevalence by 40 percent.

2. Secondary prevention: This is based on genetic screening, prenatal diagnosis of neural tube defects, and genetic counselling.

MANY NEURAL TUBE DEFECTS CAN BE PREVENTED BY PERICONCEPTIONAL FOLIC ACID, AND BY GENETIC SCREENING, PRENATAL DIAGNOSIS AND GENETIC COUNSELLING

**56-24 WHAT IS PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION?**

Folic acid is a group B vitamin. It is very cheap and safe to give as it has few and only minor side effects even in large doses.

If folic acid is given as a medicine in the form of a pill, capsule or tablet. This is called supplementation.
With periconceptional supplementation folic acid is given around the period of conception, i.e. for 3 months before and 3 months after conception. This is the recommendation. However, even if the folic acid is given for only a month, there is some benefit.

The recommended dose of folic acid to prevent the occurrence of neural tube defects is a minimum of 0.4 mg daily. This can be taken alone or in combination with other vitamins in a multivitamin tablet. One periconceptional multivitamin tablet containing folic acid a day is recommended.

Note that vitamins A and D, if given to a pregnant mother in high doses, are teratogenic and can damage the fetus. Therefore, more than one multivitamin tablet a day can be dangerous for the fetus and the mother.

**56-25 DOES A MOTHER WHO PREVIOUSLY HAD AN INFANT WITH A NEURAL TUBE DEFECT NEED MORE PERICONCEPTIONAL FOLIC ACID?**

Yes. If a mother had a previous child with a neural tube defect she is at greater risk for having another infant with a neural tube defect in future pregnancies. To reduce this increased risk for an infant with a neural tube defect it is recommended that she take 5 mg of folic acid daily for 3 months before conception and for 3 months after conception in all future pregnancies.

**56-26 IS SUPPLEMENTATION THE ONLY WAY THAT FOLIC ACID CAN BE GIVEN?**

No. As many pregnancies are not planned, it is important to put folic acid into a staple food to reduce the risk neural tube defects. When an essential nutritional factor, such as folic acid, is added to the diet of the general population in this manner, this is called food fortification. Research of folic acid fortification of flour and other wheat products (from Canada, the USA and Chile) has shown that this reduces the birth prevalence of neural tube defects.

In South Africa a law has been passed requiring the fortification of maize meal with folic acid. Many bakeries also fortify their wheat flour used for bread with folic acid. Although food fortification with folic acid is being done, it is still recommended that women take folic acid supplementation as some people may not get sufficient folic acid from fortification.

<table>
<thead>
<tr>
<th>Family relationship</th>
<th>Approximate risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>One affected sibling (brother or sister)</td>
<td>5% (1 in 20)</td>
</tr>
<tr>
<td>Two affected siblings</td>
<td>10% (1 in 10)</td>
</tr>
<tr>
<td>Three affected siblings</td>
<td>20% (1 in 5)</td>
</tr>
<tr>
<td>One affected parent</td>
<td>5% (1 in 20)</td>
</tr>
<tr>
<td>One affected second degree relative (uncle or aunt)</td>
<td>2% (1 in 50)</td>
</tr>
</tbody>
</table>

*** Research still needs to be done to see if fortification with folic acid will reduce the birth prevalence of neural tube defects in South Africa.

**56-27 WHAT ARE THE RISKS FOR A MOTHER WHO HAS AN INFANT WITH A NEURAL TUBE DEFECT HAVING A FURTHER AFFECTED CHILD?**

Women who have previously had an infant with a neural tube defect of multifactorial origin are at greater risk of having future children affected with the same type of neural tube defect. This is also true for the children of a parent who has a neural tube defect. The risks involved in these situations are:

*** With three or more affected siblings, consideration must be given to the possibility of autosomal recessive inheritance, and if the affected siblings are all male, to X-linked recessive inheritance.
Although most neural tube defects are caused by multifactorial inheritance, care must always be taken to exclude other causes of neural tube defects before genetic counselling, including risk assessment, is given.

SCREENING FOR NEURAL TUBE DEFECTS

56-28 HOW CAN NEURAL TUBE DEFECTS BE SCREENED FOR DURING PREGNANCY?

There are a number of methods which can be used to screen the fetus for neural tube defects. In countries that have well organized screening programmes, all fetuses with anencephaly and 70-80% of fetuses with spina bifida can be detected. The screening includes:

1. Maternal serum alpha-fetoprotein (AFP) screening.
2. Fetal ultrasound screening.

56-29 WHAT IS MATERNAL SERUM ALPHA-FETOPROTEIN SCREENING?

Maternal serum alpha-fetoprotein (AFP) levels are significantly raised in “open”, but not in “closed”, neural tube defects. This is why different types of neural tube defects are classified into “open” or “closed” defects. Maternal serum alpha-fetoprotein screening will miss “closed” defects.

Maternal serum alpha-fetoprotein screening is best performed at around 16 weeks (between 15 and 18 weeks) gestation on a sample of the mother’s blood. It is important to ensure that the gestational age is correct. Ultrasound dating of the fetus confirms the gestation based on the date of the last menstrual period. A raised serum level of alpha-fetoprotein indicates a high risk for an open fetal neural tube defect.

*** The maternal serum screening for Down syndrome (the Triple Test) measures the concentration of maternal alpha-fetoprotein (AFP), unconjugated oestriol (uE3) and human chorionic gonadotrophin (hCG). The level of alpha-fetoprotein in the Triple Test can be used to screen for neural tube defects.

*** Other fetal causes of a raised maternal serum alpha-fetoprotein include incorrect estimation of the gestational age, multiple pregnancy, exomphalos, nephrotic syndrome, fetal death, Turner syndrome, ectodermal dysplasia and Rhesus disease. Maternal causes include diabetes, liver or gut cancer, and hepatitis. Rarely no cause for a raised alpha fetoprotein can be found. The prognosis of these pregnancies is poor.

56-30 WHAT IS FETAL ULTRASOUND SCREENING?

It is recommended that a screening ultrasound scan for fetal abnormalities is done at 18 weeks gestation (18-23 weeks). During this scan signs of neural tube defects should be detected by an experienced ultrasonographer. Fetal ultrasound scanning can detect both open and closed neural tube defects.

Whenever a maternal serum alpha-fetoprotein (AFP) screening test is abnormal, a fetal ultrasound examination must be done to decide whether a neural tube defect or other birth defect is present or not.

*** Occasionally, the level of maternal alpha-fetoprotein is raised but a neural tube defect cannot be seen on fetal ultrasound examination. This may be because the neural tube defect is small and cannot be detected by ultrasound scan, or the raised alpha-fetoprotein is due to some other cause. In this situation the mother, preferably with her partner, should receive genetic counselling and be offered an amniocentesis. If the amniocentesis is accepted and performed, the amniotic fluid levels of alpha-fetoprotein and acetyl-cholinesterase are measured. If these are raised, and no other obvious cause for their being raised can be found, then the diagnosis can be considered to be a neural tube defect.
56-31 WHAT IS THE MANAGEMENT IF THE FETUS HAS A NEURAL TUBE DEFECT?

If a prenatal diagnosis of a neural tube defect is confirmed, the woman, preferably with her partner, should urgently receive genetic counselling regarding the diagnosis and their choices of management. For women at increased risk, or with a prenatal diagnosis of a neural tube defect, the choice of which options to take is theirs alone. Their medical care providers must respect this choice. Parents must also know that no matter what their choice, this will not influence their future routine care.

WITH GENETIC SCREENING AND PRENATAL DIAGNOSIS PEOPLE ARE ENTITLED TO GENETIC COUNSELLING AND ALWAYS HAVE THE RIGHT OF CHOICE

CASE PROBLEMS

CASE 1.

A female infant is born at term and a severe abnormality is noticed by the midwife as soon as the infant is delivered. A doctor is called to examine the infant. She notices that the top of the infant’s skull is missing and the brain is visible. The parents are told that their infant has a serious birth defect.

1. What is a neural tube defect?

It is an abnormality of the neural tube which does not close correctly towards the end of the first month after conception. The neural tube is a structure in the embryo from which the brain, spinal cord, spinal column and nerves develop.

2. What are the forms of neural tube defect which affects the brain?

   (i) Anencephaly.
   (ii) Encephalocele.

3. Which form of neural tube defect is present in this infant?

Anencephaly. This results from failure of closure of the midline of the skull, exposing the brain. The brain is always very abnormal.

4. Will this infant survive?

No. Infants with anencephaly are usually stillborn or die in the first day of life.

5. Are all infants with anencephaly females?

No. All forms of neural tube defect, including anencephaly, may occur in both male and female infants.

6. What are the clinical features of an encephalocele?

An encephalocele is less severe that anencephaly. In an encephalocele, only part of the skull does not close completely in the midline. As a result, the meninges and often part of the brain push through the hole in the skull. Unlike anencephaly, which is an open neural tube defect, encephaloceles are closed neural tube defects as they are covered with skin. The defect is usually in the occipital region but may also occur in the frontal region.

PERINATAL EDUCATION PROGRAME
CASE 2.

After delivery, a newborn infant is noticed to have an abnormality over the lower spine and also has club feet. The infant has a big head and does not move his legs. Otherwise he appears healthy and feeds well at the breast.

1. **What is the diagnosis?**

The infant has spina bifida. This is a defect in the spinal column due to failure of one or more vertebral arches to close normally. The defect is usually in the lower spine (lumbosacral region).

2. **What are the forms of spina bifida?**

   (i) Meningomyelocele.
   (ii) Meningocele.
   (iii) Spina bifida occulta.

This infant must have a meningomyelocele because the nerves to the legs have been damaged. As a result he has paralysed legs and club feet.

3. **What are the clinical features of a meningomyelocele.**

A midline mass which is covered by a thin membrane. Neural tissue is visible through the membrane. A meningomyelocele is not covered with skin.

4. **Why does this infant have a big head?**

About 80% of infants with a meningomyelocele develop a hydrocephalus. This may be present at birth but usually develops in early infancy.

5. **Why is this not a meningocoele?**

A meningocoele is a less severe defect as only the meninges bulge through the hole in the vertebral column. As there is no neural tissue in the meningocoele, there usually will be no paralysis of the legs. A meningocoele is covered with skin. Therefore, it is called a “closed” defect and would not be detected with a maternal serum alpha-fetoprotein screen.

6. **What is a spina bifida occulta?**

This is a mild form of spina bifida, which is often not noticed clinically. There is a small defect in the arch of a vertebra but the meninges do not prolapse. There may be a patch of hair or abnormal skin over the defect.

CASE 3.

A young couple, who plan to start a family, visit their general practitioner, as they want to know about neural tube defects. Their neighbour recently delivered an infant with a meningocoele. The defect was successfully corrected by surgery.

1. **How common are neural tube defects?**

In industrialized countries the prevalence of neural tube defects is about 1/1000 live births. In rural populations in South Africa, the birth prevalence is about 4/1000.
2. What is the cause of neural tube defects?

The failure of the neural tube to close normally is usually due to multifactorial inheritance. The influence of several genes, acting together with environmental factors, results in the birth defect. Rarely, the neural tube defect may be due to chromosomal or single gene defects, or teratogens.

3. What is the most important environmental factor that plays a role in causing neural tube defects?

Folic acid. A relative lack of folic acid in the diet acts together with genetic factors to result in neural tube defects.

4. How can the frequency of neural tube defects be lowered in a community?

By fortifying an essential food, such as maize meal or wheat flour, with folic acid. Fortification of maize meal in South Africa started in 2004. Many bakeries also fortify their flour used for bread.

5. What is the correct management of a child with a meningomyelocoele?

Urgent referral to a neurosurgical unit for assessment. A meningomyelocoele should be covered with sterile gauze after birth.

CASE 4

A young mother has a child with a meningomyelocoele. She and her partner want another child but are unsure of the risk of further children also having a neural tube defect. They attend a genetic clinic for counselling.

1. What is the risk of this woman having another child with a neural tube defect?

There is an increased risk if there is a family history of neural tube defects. If a previous child has a neural tube defect the risk is 5% (1 in 20).

2. How can she lower the risk of having another affected child?

She should take 5 mg folic acid daily until she falls pregnant and then continue to take folic acid until 3 months after conception.

3. How effective is periconceptional folic acid in lowering the risk for another neural tube defect?

It should significantly lower the risk of neural tube defect by 70%.

4. How can a pregnant woman be screened for a fetus with a neural tube defect?

Either with maternal serum alpha-fetoprotein screen around 16 weeks of pregnancy or by fetal ultrasound scanning at around 18 weeks of pregnancy. Ultrasound examination is also used to confirm gestational age needed for maternal serum alpha-fetoprotein screening.

5. Should all women planning a pregnancy take periconceptional supplements?

It is recommended that all women take at least 0.4 mg folic acid daily for 3 months before and 3 months after falling pregnant. This is often taken in the form of one multivitamin tablet daily. This should lower the risk of having an infant with a neural tube defect by 50%.

6. What should parents do if the fetus is found to have a neural tube defect?

They must be referred for genetic counselling.
PHOTOGRAPHS OF CHILDREN WITH NEURAL TUBE DEFECTS

Picture 56-A: Anencephaly with brain exposed.

Picture 56-B: Occipital encephalocele covered with skin.
Picture 56-C: Lumbosacral meningomyelocele with neural tissue exposed.

Picture 56-D: Lumbar meningomyelocele with only a thin membrane covering the defect.
Picture 56-E: Small sacral meningocoele covered with skin.