e-booklet: “Learning about trisomy 18”

Table of Contents

Chapter 1: Who could use this booklet

You may benefit from this booklet if you are:

- A family hearing that your baby may, or does, have trisomy 18
- A healthcare provider ordering prenatal testing or screening about trisomy 18 for your patients
- A healthcare provider giving test results about trisomy 18 to your patient
- Anyone offering support to a family learning this information about their baby

The purpose of this booklet is to:

- Provide accurate information about trisomy 18 and the testing for it in one convenient place
- Offer families and healthcare providers support

- Help begin a process – a journey – for a family learning this information about their baby
- Help open a communication dialogue between families, their healthcare providers, and others they may need during this time

QUOTE ABOUT IMPORTANCE OF OPEN COMMUNICATION/DIALOGUE BETWEEN PATIENT AND HEALTHCARE PROVIDER

Chapter 2: How did you get here?

Are you wondering how you got here?

Perhaps you are or were expecting a new baby, which is often anticipated to be a time of joy and excitement. But somewhere along the way, that changed. Maybe you received a call from your doctor or nurse, saying that a test result came back "positive" or "abnormal" for trisomy 18 in the baby. Suddenly, your pregnancy became "high-risk" and you were offered more tests or information. Maybe you wanted to learn more about trisomy 18 or the testing – but you likely became more anxious or worried. Although these feelings are normal given the circumstances, they can be very difficult to experience and work through.

QUOTE FROM FAMILY HEARING POSITIVE SCREEN AND DIAGNOSTIC RESULTS FOR T18

Depending upon what results you heard, there may or may not be anything wrong with your baby. Perhaps a flag has been raised by a screening result for trisomy 18, which is not meant to give you a "yes" or "no " answer. The key point is that you probably need more information to understand the details. While you may find of it some here, more may come from your doctor, a genetic counselor, or another healthcare professional.

As you learn more, you may feel like you are learning a "new language," one that you never thought you would need to speak. As difficult as it may seem, do not hesitate to ask for more facts or support. The dialogue you have with your healthcare professional and those who

support you will help you on your journey to healing.

Chapter 3: What is trisomy 18?

A little background on trisomy 18

Also known as Edwards syndrome, trisomy 18 is a relatively common genetic condition caused by the presence of an extra information from chromosome 18.[1] Two doctors and their colleagues first described it in 1960, based on medical signs commonly seen in several children.[2] Trisomy 18 occurs worldwide, and estimated to occur in about 1/3,600 - 1/10,00 live born babies per year.[3] On average, it is thought to occur in about 1/6,000 babies a year.[4]

Most with trisomy 18 have three full copies of chromosome 18 in their cells. More will be described about chromosomes later in this section, but having this extra chromosomal material can cause a variety of medical signs and symptoms. These vary from person to person, but can include:

Table 2. Characteristics of trisomy 18

Characteristics (some may be present prenatally)[1]
Small growth
Specific facial characteristics
A specific hand posture, with overlapping fingers
Underdeveloped finger and toenails
Short hallux (big toe)
Short sternum (breastbone)
Heart structure problems
Kidney development problems
Gastrointestinal problems
Brain development problems
Cleft lip or cleft palate (hole/opening in lip or roof of mouth)
Eye development problems
Limb development problems

What are chromosomes?

Chromosomes are structures found in nearly every cell of our body. They contain our genes, which contain instructions for all our various traits (like eye color, hair color, our growth and development). We usually have 46 chromosomes in total in our cells, including one X and one Y chromosome in males, and two X chromosomes in females. Parents usually give half their chromosomes (and genes) randomly to their children.

Those with trisomy 18 most often (about 94%) have three copies of an entire chromosome 18 in all their cells.[1] In fewer than 5%, they have what is called "mosaic" trisomy 18 – meaning that the extra chromosome 18 is only in a portion, but not all, of their cells. Finally, a small portion of individuals with characteristics like trisomy 18 may have "partial" trisomy 18. In this scenario, they have extra material from chromosome 18 in their cells, but it is not the entire chromosome. In all situations, the extra information from chromosome 18 in their cells leads to the medical concerns an individual may have.

How does trisomy 18 happen?

If someone has full trisomy 18 (trisomy 18 in all their cells), this usually happens because of a process called non-disjunction. This is an uneven division of a mother or father's chromosomes during cell division, which happens randomly at conception. If a cell unevenly divides its chromosomes, an extra one can get passed along to a child. If it happens to be the 18^{th} chromosome, that child would have trisomy 18. This happens a bit more often to women that are over age 35-40 at the time their child is due.

If non-disjunction of chromosome 18 happens after a pregnancy is conceived, it can result in trisomy 18 in only a portion of the baby's cells (or mosaic trisomy 18). Sometimes, signs and symptoms may be milder in people with mosaic trisomy 18 because the extra chromosome material is not in every cell.

If someone has partial trisomy 18, this usually happens because of a mother or father carrying a physical difference (or rearrangement) of their chromosomes. These rearrangements are

called translocations or inversions, and may cause no symptoms whatsoever in the parent. This is because all the chromosome information is there (and "balanced"), but is just not in the usual place. However, this information may become "unbalanced" when they go on to have a child.

In any of these situations, it is never a mother's or father's fault that their child has trisomy 18. The processes of cell and chromosome division are completely outside a parent's control, and occur randomly. Although non-disjunction can happen more often in women as they get older, it is still not anyone's fault if it happens and there is no current way to remove the extra information from one's cells. Most times, trisomy 18 occurs in a family randomly. The chance of it happening again to a couple is usually low (perhaps 1%), but a medical professional like a genetic counselor is the best person to estimate this for them.

When is trisomy 18 diagnosed?

If some signs are seen during a prenatal ultrasound, concerns may be raised about a baby having trisomy 18. QUOTE FROM FAMILY RECEIVING THIS INFORMATION BASED ON ULTRASOUND FINDINGS. Concerns may also be raised based on prenatal screening results. Referrals may be then be made to get more information about the pregnancy, such for more ultrasounds (like a fetal echocardiogram or more detailed ultrasounds), to see a maternal-fetal medicine specialist, to see a genetic counselor, or to see other specialists. Those will be discussed in Chapter 6. Most people ultimately learn their child has trisomy 18 during a pregnancy.

Unfortunately, most pregnancies with trisomy 18 have a high risk of fetal loss, stillbirth and a baby passing away in early life.[5] QUOTE FROM A FAMILY THAT LOST THEIR LITTLE ONE. However, some children survive for several years after birth. Deliveries may be straightforward, or more complex and needing additional supports (such as the availability of pediatric medical specialists), depending on what is going on for the baby.

Although it is more rare, some with full trisomy 18 can live for several years. Historically, there has unfortunately been a grim prognosis given to families of these children. And while these

children often have significant health concerns (like heart conditions, significant intellectual disabilities, respiratory issues, feeding challenges) and their overall size as a group is very small, increased medical interventions continue to offer hope for these families.[6] QUOTE FROM FAMILY WHOSE CHILD SURVIVED BEYOND WHEN WHAT WAS PREDICTED.

Chapter 4: How is the possibility of trisomy 18 discovered in a pregnancy?

Prenatal genetic screening

Some health problems are caused by problems related to the chromosomes. Prenatal genetic screening is targeted to some types of aneuploidy, situations in which there are missing or extra chromosomes.[7] Prenatal genetic screening is an optional way to get information about the possibility of specific genetic conditions (like trisomy 18) in a pregnancy, and may be the first time a concern comes up about trisomy 18. Screening is not meant to give a definitive "yes" or "no" answer – even if someone receives a "screen positive" result. Screening gives a chance or probability for these things to happen, and the chance may be higher or lower than expected, or exactly as expected. Screening does not provide a diagnosis. Prenatal diagnostic testing for genetic conditions will be discussed in Chapter 5.

Available prenatal genetic screening options

These vary by area, center and healthcare provider. There are several options, each with their own benefits and limitations. Another option is to do no prenatal screening. These decisions are very personal, and there are no right or wrong decisions for any family.

Key aspects of each are summarized in the table below. QUOTES FROM FAMILIES THAT HAVE CHOSEN SOME OF THESE OPTIONS, AND ONE THAT HAS NOT DONE SCREENING.

Table 2. Comparison of prenatal genetic screening options in single (not multiple) pregnancies

	Non-invasive prenatal testing (NIPT)[8]	First-trimester combined screening[7, 9]	Second-trimester "triple screen"[7, 9]	Second-trimester "quad" screen[7, 9]	Integrated screening (with ultrasound)[B,7, 9]	Sequential screening (step-wise)[C,7, 9]	Detailed two-dimensional ultrasound (or fetal anatomy scan, genetic sonogram)
When done in a pregnancy	About 10-22 weeks	11-just before 14 weeks	15-20 weeks	15-20 weeks	11-13 weeks and 15-20 weeks	11-13 weeks and possibly 15-20 weeks	18-22 weeks
Best group of women for screen	Those at "higher risk"[A]	Any	Any	Any	Any	Any	Any
What is done	Fetal DNA in mother's blood is studied for comparison studies	Two chemicals in mother's blood studied and nuchal translucency (NT) ultrasound	Three chemicals in mother's blood studied	Four chemicals in mother's blood studied	One chemical studied in mother's blood and NT ultrasound in first trimester; quad screen in second trimester	Same as for first-trimester combined screening and possibly second-trimester screening (if negative results)	Prenatal ultrasound of greater detail is performed
How it is done	Mother's blood is drawn	Mother's blood is drawn, NT ultrasound is done	Mother's blood is drawn	Mother's blood is drawn	Mother's blood is drawn twice, NT ultrasound is done	Mother's blood is drawn (perhaps twice), NT ultrasound is done	Sound waves are used to create an image on a screen and examine the anatomy of the baby
What can be learned	Chance for Down syndrome, trisomy 18, others (depending on	Chance for Down syndrome, trisomy 13, trisomy 18	Chance for Down syndrome, open neural tube disorders,	Chance for Down syndrome, open neural tube disorders,	Chance for Down syndrome, open neural tube disorders, trisomy	Chance for Down syndrome, open neural tube disorders,	Several obvious changes to the baby's growth and development

	testing laboratory)		trisomy 18	trisomy 18	18	trisomy 18	
Timeframe for results	7-10 days	7-10 days	7-10 days	7-10 days	4+ weeks	1-4+ weeks	Instantly to 7-10 days
Accuracy	~99% for Down syndrome and trisomy 18	82-87% for Down syndrome, ~90% for trisomy 18	~69% for Down syndrome	~81% for Down syndrome, ~85% for open neural tube disorders, ~75% for trisomy 18	94-96% for Down syndrome	~95% for Down syndrome	50-75% for Down syndrome
Risks	Related to blood draw, (none for baby)	Related to blood draw (none for baby)	Related to blood draw (none for baby)	Related to blood draw (none for baby)	Related to blood draw (none for baby)	Related to blood draw (none for baby)	None for mother or baby
Benefits	Highly accurate screen for specific chromosome conditions; Can be done early; No risk to baby	Can be done early; No risk to baby	No risk to baby	No risk to baby	No risk to baby	No risk to baby	Can get detailed information about growth/development of baby; No risk to mother or baby
Limitations	Prenatal diagnosis needed for confirmation of abnormal results; May not be covered by insurance; Not widely available; May	Screens for certain chromosomes and no open neural tube disorders	Screens for certain chromosomes	Screens for certain chromosomes	Screens for certain chromosomes; Several appointments and waiting can be challenging	Screens for certain chromosomes; Several appointments and waiting can be challenging	Not 100% sensitive; some things can be missed on an ultrasound.

	have to repeat if not enough fetal DNA; Screens for certain chromosomes and no open neural tube disorders						

A: Those over age 35-40 at time of baby's birth, with abnormal prenatal screening results, with specific concerns found on prenatal ultrasound, or with a family history of Down syndrome or other chromosome condition. B: Can also be done without ultrasound; accuracy for Down syndrome is 85-88% with this method. C: Can also be done in a "contingent" manner. If first-trimester combined screening results are positive, diagnostic test is offered. If negative, no further testing is offered. If intermediate, second-trimester screening is offered. Accuracy for Down syndrome is then 88-94% with this method.

Chapter 5: How is trisomy 18 diagnosed in a pregnancy?

Prenatal diagnosis procedures

Prenatal diagnosis can be for aneuploidy or a different genetic condition. Either way, it is meant to give a definitive "yes" or "no" answer. The actual options vary by area, center and healthcare provider. There are two options, each with its own benefits and limitations. Another option is not to have a prenatal diagnosis procedure. These decisions are very personal, and there are no right or wrong ones for a family.

Families choose to have prenatal diagnostic procedures for different reasons, and these may include having information to make difficult decisions about the pregnancy. These decisions may include choosing to say a loving goodbye early to their baby by interrupting the pregnancy, or perhaps planning for their baby's delivery, birth and life – even if that life is expected to be brief. More details about these decisions are discussed in Chapter 7. QUOTES

FROM FAMILIES THAT CHOSE THESE DIAGNOSTIC PROCEDURES, AND ONE FROM A FAMILY THAT DID NOT.

Key aspects of each choice are summarized in the table below.

Table 2. Comparison of prenatal diagnosis procedures

	Chorionic villus sampling (CVS)[10]	Genetic amniocentesis (Amnio)[A,11]
When done in a pregnancy	About 10-13 weeks	About 15+ weeks
Target group of women	Those at "higher risk"[B]	Those at "higher risk"[B]
What is done	Fetal chromosomes are studied for aneuploidy (like Down syndrome)	Fetal chromosomes and amniotic fluid are studied for aneuploidy and open neural tube disorders
How it is done	An ultrasound-guided catheter is inserted through the cervix or abdomen of the mother to study placenta cells	An ultrasound-guided needle is inserted into the abdomen of the mother
What can be learned	Complete, general chromosome makeup of the baby (including gender)	Complete, general chromosome makeup of the baby and risk for open neural tube disorders
Timeframe for results	About 2-4 weeks	About 2-4 weeks
Accuracy	>99% for aneuploidy	>99% for aneuploidy, >98% for open neural tube disorders
Risks	About 1% for miscarriage, infection, bleeding; About 1% risk for inconclusive results; Parents may need blood drawn depending on results; May need to be repeated if cells do not grow in laboratory	About 0.5% for miscarriage, infection, bleeding, fluid leakage; Parents may need blood drawn depending on results; May need to be repeated if cells do not grow in laboratory
Benefits	"Yes" or "no" about baby's chromosomes; Done earlier than amniocentesis	"Yes" or "no" about baby's chromosomes
Limitations	No information about neural tube disorders	Does not test for every existing genetic condition

A: Amniocentesis done for genetic testing purposes, as opposed to other reasons the procedure may be done. B: Those over age 35-40 at time of baby's birth, with abnormal prenatal screening results, with specific concerns found on prenatal ultrasound, or with a family history of Down syndrome or other genetic condition.

Chapter 6: Referrals you may be offered

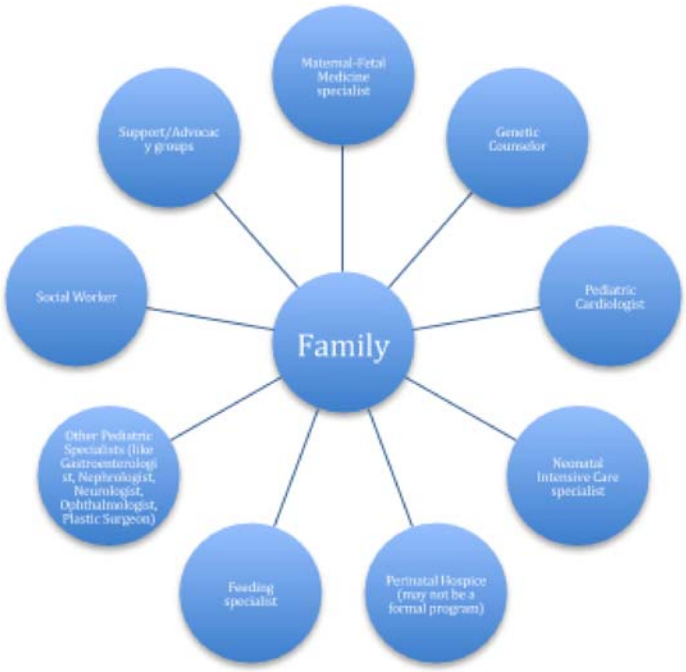
If your baby may have trisomy 18, or does have it, you may be offered a number of referrals to

see specialists. These will vary depending on what is going on for the baby, what decisions you may make about the pregnancy, and how many medical specialists you might like to see. This chapter will cover what you might expect from visits to see these individuals. FAMILY QUOTES FROM PEOPLE THAT HAVE HAD SOME OF THESE REFERRALS.

- **Maternal-Fetal Medicine specialist/Perinatologist**
    - This specialized obstetrician can help you better understand what is going on, medically, for the baby. He or she may also help care for you and your pregnancy going forward. They may recommend further procedures, such as a dedicated ultrasound of the baby's heart (fetal echocardiogram), more detailed ultrasounds, or other specialized prenatal tests. These will vary depending on what is going on for the baby.
- **Genetic Counselor**
    - This specialized medical professional can help you understand any prenatal screening/diagnostic test results you have had. He or she will review the genetics and medical aspects of trisomy 18. They will likely want to discuss your family history, to see whether trisomy 18 or any other genetic conditions may impact you and/or your close relatives. If you would like to know, they will also talk about the chance of having another baby with trisomy 18 in the future. They may also suggest advocacy groups for you to get more information and find support.
- **Support/Advocacy groups**
    - These groups involve parents/families in a similar situation, medical professionals and others who offer support. They are good places to get more information, hear other perspectives, and feel less alone. Specific examples are listed in Chapter 9.
- **Pediatric Cardiologist**
    - This specialized pediatric doctor will help you better understand what is going on for your baby's heart, if there is a problem. He or she may also make recommendations for your pregnancy, delivery, and follow your baby after birth. Their degree of involvement will depend on what is going on for the baby.
- **Neonatologist**

    - This specialized pediatric doctor works with a team in the Neonatal Intensive Care Unit of a hospital, providing care to babies needing significant medical care after birth. He or she may make recommendations for your pregnancy, delivery, and follow your baby after birth. They/their team may also help arrange an NICU orientation at the hospital for you.
- **Perinatal Hospice**
    - This may/may not be a formal program at the hospital, but the goal is to offer support to those continuing a pregnancy in which a baby's life is expected to be brief. This approach walks with these families on their journey through pregnancy, birth, and death, honoring the baby as well as the baby's family.[12]
- **Feeding Specialist**
    - This specialized medical professional often works with a team to help you better understand challenges your baby may have with feeding. He or she may follow your baby after delivery and birth.
- **Social Worker**
    - This specialized medical professional often works with a team to help support you during your pregnancy, and potentially your delivery and after birth. They may connect you with helpful resources and advocate for you/your family.
- **Other Pediatric Specialists**
    - Generally, they may make recommendations for your pregnancy, delivery, and follow your baby after birth. Their degree of involvement will depend on what is going on for the baby.
    - Pediatric Gastroenterologist: This specialized pediatric doctor will help you better understand what is going on for your baby's digestive system.
    - Pediatric Nephrologist: This specialized pediatric doctor will help you better understand what is going on for your baby's kidneys.
    - Pediatric Neurologist: This specialized pediatric doctor will help you better understand what is going on for your baby's brain.
    - Pediatric Ophthalmologist: This specialized pediatric doctor will help you better understand what is going on for your baby's eyes and vision.
    - Plastic Surgeon: This specialized doctor will help you better understand your baby's cleft lip and/or palate, if there is one.

Figure 1. Schematic of family and possible medical specialists they may see



Chapter 7: Making decisions

You've learned that your baby has trisomy 18

You might have heard that your baby has trisomy 18 from a number of individuals: your primary care doctor, obstetrician, genetic counselor, Maternal-Fetal medicine specialist, or someone else. No matter who told you, everything changed when it happened. And now you may be faced with some challenging, emotional decisions. Or perhaps you've already made them.

This is not an easy time for any family, and others may not fully understand whatever decision you choose. You may feel alone in your choice, but reaching out for support from others (if/when you are ready) can be healing. Alternatively, you may want to keep information to

yourself and draw on your inner strength. Be sure to have an ongoing dialogue with your doctor, though, especially if you need help through this. He or she is there to support you, and can also help you access mental health or other resources if you need them. There will be bad days and, hopefully, there will be fewer of them with time. Healing does not come overnight; it is part of an ongoing process that follows a very individual path. More resources are discussed in Chapter 9.

Remember that no matter what you choose, there is no wrong decision if you do what is right for you. QUOTES FROM FAMILY CHOOSING EACH DECISION.

Choosing to say a loving goodbye early – interrupting the pregnancy

After much consideration, you have made the difficult decision to interrupt the pregnancy and say goodbye to your baby far too early.

Depending on how far along you are in the pregnancy, you may have a specific procedure to interrupt the pregnancy. The person doing the procedure varies with your area and the center where you are going.

After 12 weeks of pregnancy a dilation and evacuation (D&E) procedure may be done. For this, the contents of the uterus are removed by a suction device that is inserted into the uterus. It may also be called a vacuum curettage. Rarely, the pregnancy is not completely removed and bleeding/infection/other complications and side effects can occur.[13] Unfortunately, you will not be able to see your baby if this procedure is done. If this is important to you so you can take photographs, have a memorial or other service, or other reason talk to your doctor about the possibility of having an induced labor to be able to see your baby.

Later in pregnancy, labor may be induced. Once labor begins, a regular delivery and pregnancy interruption can occur. You can usually see your baby if this happens.

Choosing to allow a natural (and possibly short) life – continuing the pregnancy

After much consideration, you have made the difficult decision to continue the pregnancy, choosing to allow what might be a short life for your baby. You may choose to pursue referrals mentioned in Chapter 6. These may help you prepare for the rest of your pregnancy, delivery, and your baby's life after birth. You and your family may well need support, and this is very natural. You may need help saying a loving goodbye to your baby – whenever it may happen – which can involve taking photos, having a service, and otherwise honoring your baby.

Chapter 8: Where do you go from here?

This may be a very taxing time for you and your family, which should be respected and acknowledged. But it is also the beginning of a journey, and a process to healing. This booklet will hopefully help with that process.

You may have to answer a lot of questions from family, friends and others in your support network. Some of them may not understand things completely, including decisions you have made about the pregnancy. They may sometimes ask questions out of curiosity or ignorance, but this is often out of a desire to support you and your loved ones. Feel free to bring people you find supportive to appointments, send them to online resources you have been directed to, or share medical documents with them. Support and advocacy groups can also be helpful. More specific resources for how to navigate this part of the journey can be found in Chapter 9.

This booklet is intended to help you begin a conversation, a dialogue, with your healthcare professionals and loved ones. They are there to care for you through whatever decisions you make, regardless of their own beliefs. Couples and families that open themselves to this support – from their medical, personal and advocacy support systems – make the journey to healing more smoothly.

"Every child's life, no matter how fragile their life or brief their days, forever changes our world." -- Victoria Miller

Chapter 9: Resources

T18F website

Other support group websites

A Time to Decide, A Time to Heal

Resources for how to tell others about a medical diagnosis, decisions

Chapter 10: References

---

1. Cereda, A.; Carey, J. C., The trisomy 18 syndrome. *Orphanet journal of rare diseases* **2012,** *7*, 81.
2. (a) Edwards, J. H.; Harnden, D. G.; Cameron, A. H.; Crosse, V. M.; Wolff, O. H., A new trisomic syndrome. *Lancet* **1960,** *1* (7128), 787-90; (b) Smith, D. W.; Patau, K.; Therman, E.; Inhorn, S. L., A new autosomal trisomy syndrome: multiple congenital anomalies caused by an extra chromosome. *The Journal of pediatrics* **1960,** *57*, 338-45.
3. Root, S.; Carey, J. C., Survival in trisomy 18. *American journal of medical genetics* **1994,** *49* (2), 170-4.
4. Embleton, N. D.; Wyllie, J. P.; Wright, M. J.; Burn, J.; Hunter, S., Natural history of trisomy 18. *Archives of disease in childhood. Fetal and neonatal edition* **1996,** *75* (1), F38-41.
5. (a) Morris, J. K.; Savva, G. M., The risk of fetal loss following a prenatal diagnosis of trisomy 13 or trisomy 18. *American journal of medical genetics. Part A* **2008,** *146* (7), 827-32; (b) Won, R. H.; Currier, R. J.; Lorey, F.; Towner, D. R., The timing of demise in fetuses with trisomy 21 and trisomy 18. *Prenatal diagnosis* **2005,** *25* (7), 608-11.
6. Bruns, D.; Campbell, E., Twenty-two survivors over the age of 1 year with full trisomy 18: presenting and current medical conditions. *American journal of medical genetics. Part A* **2014,** *164A* (3), 610-9.
7. Gynecologists, T. A. C. o. O. a., Screening Tests for Birth Defects http://www.acog.org/~/media/For%20Patients/faq165.pdf?dmc=1&ts=20140423T1514393293. 2014.
8. National Coalition for Health Professional Education in Genetics, N. S. o. G. C., Non-Invasive Prenatal Testing (NIPT) Factsheet http://www.nchpeg.org/index.php?option=com_content&view=article&id=384&Itemid=255. 2012.
9. ACOG Practice Bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstetrics and gynecology* **2007,** *109* (1), 217-27.
10. Dimes, M. o. Chorionic villus sampling http://www.marchofdimes.com/pregnancy/chorionic-villus-sampling.aspx.

http://www.marchofdimes.com/pregnancy/chorionic-villus-sampling.aspx (accessed April 23, 2014).
11. Dimes, M. o. Amniocentesis http://www.marchofdimes.com/pregnancy/amniocentesis.aspx. http://www.marchofdimes.com/pregnancy/amniocentesis.aspx (accessed April 23, 2014).
12. Perinatal Hospice and Palliative Care: A Gift of Time. http://perinatalhospice.org/Perinatal_hospices.html (accessed April 23, 2014).
13. Gynecologists, A. C. o. O. a., Induced Abortion. 2011.