SICKLE CELL DISEASE: GENETICS AND ETHICAL ISSUES

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Sickle cell disease (SCD) describes a group of hemoglobinopathies characterized by a single amino acid substitution in the beta globin chain (Hammerman, 2011).
Patients with \( \beta \), \( b \), or \( b-\beta\)-thal have inherited a sickle \( (\beta) \) gene from one parent and an \( , \), or \( \beta\)-thal assembla gene from the other (Andolfi, ).
Hemoglobin results from the substitution of a valine for glutamic acid as the sixth amino acid of the beta globin chain (Hammerman, 2011).
I
NTRODUCTION

Sickle-cell anemia (HbSS) results from inheriting mutant hemoglobin (Hb) from both parents. (Randolph, 2007; WHO, 2006).
Sickle Cell Disease prevalence

- affects ~ 1 in 360,000 African Americans
- in Hispanic births
- in Central Americans
- Mediterraneans

(CDC, 2011; Randolph, 2007).
Sickle cell disease

Diagnosis

Sickle cell test & hemoglobin electrophoresis
- Screening and diagnosis

Renatal testing - pre-implanted zygote
-chorionic villus sampling – 1st trimester
-amniocentesis – 2nd trimester

(Quinn & Ackman, ).
How is it inherited?

- The genes that code for the globin chains are located at specific loci on chromosomes 16 and 11 (Rolph, 2007).
How is it inherited?

- The α-like genes ($\alpha$ and $\zeta$) are located on chromosome 16, whereas the β-like genes ($\beta$, $\gamma$, $\varepsilon$, $\delta$) are located on the short arm of chromosome 11 (Randoolph, 2007).
How is it inherited?

- β hemoglobin variants are inherited as autosomal codominants, with one gene inherited from each parent (Andolph, ).
How is it inherited?

- Homozygous (bb), inherited a sickle (S) gene from one parent and another gene from the other parent.

- Heterozygous (Bb), inherited only a sickle (S) gene from one parent (andol...)

Key: [AA] Normal 25%
[SS] Disease 25%
[AS] Carrier 50%
Is SCD not multifactorial? (environment does not contribute to its inheritance) However, environment can contribute to its severity.

- Low environmental oxygen level → sickling
A change in a single amino acid is a missense mutation.

- DNA template strand →
- Transcription ↓
- Translation

Source: http://canada.canacad.ac.jp/BiologyIBHL1/1295?view=print
Molecular Basis for Disease: Altered Beta Globin Polypeptide Sequence

Source: http://www.sciencecourseware.com/blol/screenshot/hemolab.html
Substitution of amino acid valine for the glutamic acid (sixth amino acid in beta globin poly peptide chain)

At DNA level, change was $\rightarrow$ to, corresponding to $\nwarrow$ codons and

(ewis, )
What happens ...

- A line at the 6th position changes the surface of hemoglobin molecules so in low oxygen conditions they attach at many more points than they would with glutamic acid

(Lewis, 2007)
The aggregated hemoglobin molecules form ropelike cables that bend into rigid, fragile, sickle-shaped structures which lodge in narrow blood vessels, cutting off local blood supply.

(LeWiss, 2007)
With blockage → sickling speeds up, as oxygen level falls.

Resulting:
- Pain in blocked body parts (hands, feet, intestines)
- Ones ache
-reat fatigues

(, )
*Symptoms*:

- Vaso-occlusive/pain crises
- Bacterial infections (childhood)
- Chronic hemolytic anemia
- Plastic episodes (bone marrow failure)
- Cardiac defects e.g. enlarged heart, murmurs
- Reduced growth
- Complicated pregnancies
- Sickle cell trait (asymptomatic) (Randolph, 2007)
Testing for inheritance of SCD:ickle cell test & electromyography

electrophoresis
  - screening and diagnosing

Renatal testing - pre-implanted zygote
  - chorionic villus sampling – 1st trimester
  - amniocentesis – 2nd trimester

(Quinn & Ackerman, 2010).
Sickle cell test - presence of sickle hemoglobin

Hemoglobin electrophoresis - separates different hemoglobins

confirmatory

Factors affecting result

- Blood transfusion - past 4 months false-negative

- Age < 6 months false-negative

- or et al. hemoglobin present.
SICKLE CELL DISEASE

TREATMENTS

Supportive:
- Hydration
- Vitamin
- Oxygen
- Analgesics
- Antibiotic

Transfusions
- Prevention
  - Sequestration and aplastic crises
  - Treatment
    - Cute chest episodes
    - Maintenance
- Pregnancy
- Re-surgery

Bone marrow transplantation
- Children - severe complications - stroke

Hydroxyurea (adults)
- Increasing b. proportion
Harmonics

- Hydroxyurea

Cutting Edge

- Life-long cure = hematopoietic stem cell transplantation
- Limited to < age 16; b/c toxicities/death if older

( Field, Vichinsky, & DeBaun, 2011; Khan & Rodgers, 2011)
Cutting edge cont.

- Hematopoietic stem cell transplantation is performed - if HLA-matched sibling donor exists
- < % eligible patients
- Subject's HLA-matched siblings have ineligible as donors
- **atri:**
  - year-old
  - African American female
  - + pregnancy (2 months)
  - husband has sickle cell disease
  - genetic counseling:
    - %(b) + %(b)
  - wants prenatal diagnosis
  - considering abortion
  - husband not
  - siblings with
renat al di agnosisi
result:
sickle cell disease positive
hat . ext ???
Is it right to terminate an innocent life?

Is the fetus a person with moral and legal rights?

When does personhood begin?

(Lo, 2009)
M A I N  E T H I C A L  P R I N C I P L E S

- P R E N A T A L - J U S T I C E

- R E S P E C T  O F  P E R S O N
- B E N E F I C I E N C E
- N O N M A L  E F F I C I E N C E
- C O N S E N T
\textbf{ETHICAL DILEMMA & TAKEHOLDERS}

- Is abortion right?
- Why deliver baby to suffer? Beneficence
- Should health provider be forced to care for women undergoing abortion? —
  \texttt{\textbackslash respect of persons\textbackslash confidentiality\textbackslash privacy}
- An father of baby object?
- Who pays justice
<table>
<thead>
<tr>
<th>SUPPORTERS</th>
<th>OPONENTS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women will still choose to terminate pregnancies whether abortion is legal or not. Universal right, and avoid unacceptable risks.</td>
<td>Not (Kohn, 2009; Scotland, 2011).</td>
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<tr>
<td><strong>Supporters</strong></td>
<td><strong>Opponents:</strong></td>
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<td>No evidence of psychiatric problems; very low incidence of clear psychiatric illness stem from circumstances leading to abortion, not just abortion (Kwon, 2009; Scotland, 2011).</td>
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<td>Forced pregnancy and motherhood undermines women’s equality</td>
<td>Abortion rights hinder women’s equality</td>
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<td>- “wombless” male body as normative.</td>
<td>- Not merely argument for abortion rights (Achichoch, )</td>
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<td>Qual citizenship defined</td>
<td></td>
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<tr>
<td>AMERICANS - CATHOLICS and WHITE EVANGELICAL PROTESTANTS - POSSIBLE TO DISAGREE TEACHINGS (ANKS, ).</td>
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<tr>
<td>CHURCH HOSPITALS PROHIBIT PRACTICING &quot;DIRECT ABORTION&quot;</td>
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<td>TERMINATION BEFORE OR AFTER VIABILITY ('O'Rourke, ).</td>
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<tr>
<td>&quot;YOU SHALT NOT KILL&quot; (EXODUS : , ).</td>
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<tr>
<td>bsol ut ist s (left)</td>
<td>radual ist (middle)</td>
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<tr>
<td>always ethically permissible,</td>
<td>human beings gain rights as they age.</td>
</tr>
<tr>
<td>vote –.</td>
<td>drive -.</td>
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<tr>
<td>alcohol –.</td>
<td>senator –.</td>
</tr>
<tr>
<td>resident – age.</td>
<td>right to life – sometime between conception and birth (Kaczor, ).</td>
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</table>
 Roe v. Wade - abortion legalized.


Planned Parenthood of Central Missouri v. Danforth's right to know unconstitutional.

(Lehn & Adath, Lewis, Legal Information Institute (LII), n.d.)
PERSONAL DECISION

HOW BEST TO DEAL WITH DILEMMA

- Full explanation – Keep promises
- Honesty
- Informed decision
- Options
- Adoption?
- Professional’s dilemma
- Values
- Obligation
- Autonomy
- Male partner support
- Privacy
- Confidentiality
- Respect of persons
- Lutamic acid to aline
- et al genetic disorder = thical dilemma
- 
- responsibilities
  
  - woman: unborn (beneficence; nonmal efficience)
  
  - health care providers
    
    - represent unborn (beneficence)
    - respect of persons
    - autonomy
    - confidentiality
    - informed consent
    - provider conflict?

- (o, p; ,).


CDC (2011) *Sickle Cell Disease (SCD)*. Retrieved from http

http://www.cdc.gov/NCBDDD/sicklecell/data.html


Case Consultation
Worksheet A

Step 1: Personal Responses
I am opposed to abortion in the case of a sickle cell fetus. I believe that a sickle cell child can live a relatively healthy life if the family gets the proper information needed to care for that child. Children should be given a chance to live life and to survive no matter the result of prenatal testing. Sometimes the experience of having cared for a sick child brings out the humanity and deep caring abilities that make people better human beings.

Step 2: Facts of the Case
1. Kati’s prenatal test shows that the fetus has sickle cell disease
2. Kati wants to get an abortion
3. The husband is opposed to abortion but realizes that he has no right to stop his wife; he loves his wife and wants to support her decision.
4. The clinic does not perform elective or therapeutic abortions, so Kati was referred to an abortion clinic.

Step 3a: Clinical/Psychosocial Issues Influencing Decision
- Is it right to terminate an innocent life?
- Is the fetus a person with moral and legal rights?
- When does personhood begin?
- Is it right to bring a child to a world of suffering, agony, and untimely death?
- Should a health provider be forced to care for a woman undergoing abortion even when her beliefs are against it?
- Can the father of the baby stop the woman from a decision to abort?

Step 3b: Initial Plan
Create a welcoming environment for patient and husband
Include the husband in consultation when appropriate
Do pregnancy test to confirm pregnancy
Explain prenatal testing
Get consent for and refer patient to lab for prenatal testing
Explain result to patient
Explain sickle cell disease management and be truthful and realistic while explaining expected pregnancy outcomes.
If patient insists on abortion refer to skilled abortion clinic
Explain the abortion process
Answer every question
Acknowledge the grief patient may experience
Provide counseling services
Step 4: Policies & Ethical Code Directive

1. Autonomy: When a woman is faced with the choice of abortion, she has the right to be informed of every benefit and or dangers associated with the procedures. The patient should be given the opportunity to make autonomous and supported decisions about a problem pregnancy (Scotland, 2011).

2. Respect for persons: This includes respecting other people’s preferences and values as well as treating them with compassion and dignity (Lo, 2009; p.11). The provider should respect the woman’s decision.

3. Beneficence: Acting in the best interest of the patient is described as the principle of beneficence. Kati’s best interest is to have the full information about her situation in order to make the best informed decision for herself and the baby.

4. Do-no-harm: The health care providers have the obligation to represent the interest of the unborn children so that they have the best opportunity to grow well without harm (Lo, 2009, p 286). Educating the mother helps her make the best decision for herself and the unborn child.

5. Justice: Patient cannot be denied access to abortion no matter how much her opinion and beliefs differ from those of the providers

6. Confidentiality: Patient’s information should be handled with caution making sure that her privacy is maintained. If the patient does not want her spouse to know about her decision, that should be respected and her records should be kept confidential.

7. Consent: Patients require full explanation of intervention, benefits, risks, consequences of intervention, consequences of no intervention, as well as alternative interventions in other to give a well informed consent (Lo, 2009; p. 22).

Step 5: Ethical Principles Analysis

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<td>Absolutist defenders of abortion believe that</td>
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Outline of Ethical Argument

Supporters of abortion

- Women will still choose to terminate pregnancies whether abortion is legal or not.
- Make abortion a universal right, and avoid unacceptable risks
- No evidence of psychiatric problems; very low incidence of clear psychiatric illness stem from circumstances leading to abortion not abortion
- Forced pregnancy and motherhood undermines the equality for women
- The Catholic Church hospitals prohibit practice of “Direct abortion” because of their religious beliefs.

Opponents of abortion

- Universal access to abortion increases the rate of unwarranted abortions
- Association with depression and anxiety
- Abortion rights hinder the equality of women and promote cultural hostility toward pregnancy and motherhood (Bachioch, 2011).
- Some believe it is possible to disagree with their religion's teachings on abortion and still remain in good standing with their faith (Banks, 2011).
- Absolutist critics of abortion believe that
APPENDIX B
CASE CONSULTATION
WORKSHEET B

Plan & Implementation Strategy:
Comprehensive patient history
Complete physical examination
Obtain confirmation of pregnancy
The gestational age should be determined
Ultrasound examination
Explain prenatal testing
Get consent for and refer patient to lab for prenatal testing
Explain result to patient
Explain sickle cell disease management and be truthful and realistic while explaining expected pregnancy outcomes.
If patient insists on abortion refer to skilled abortion clinic

At The Abortion Clinic:
Create a welcoming environment for patient and husband
Include the husband in consultation when appropriate
Explain the abortion process
Answer every question
Antibiotic prophylaxis
Hematocrit (or hemoglobin) and Rh(D) status
Mifepristone (RU-486)
Surgical curettage/extraction procedures
Systemic abortifacients
Cervical preparation
Nonsurgical methods in conjunction with surgical techniques
Acknowledge the grief patient may experience
Provide counseling services
Provide follow up services
Advances Clinical/Psychosocial Interests:

Good history taking, physical exam, and tests enable the providers to confirm patient’s pregnancy, age of gestation, and assesses the general condition of the patient which will help in determining the options she has in her decision making. Explaining prenatal testing as well as the result to patient also helps the patient to get the information needed for her decision making.

Providing counseling services and follow up services for patient and family helps them to better deal with the emotional stress from her situation and her decision.

At the abortion clinic, antibiotic prophylaxis is recommended because it significantly reduces the frequency of postabortal endometritis (Shulman, & Ling, 2011).

Adheres to agency policies and professional ethics codes:

If patient insists on abortion, referral to skilled abortion clinic is part of agency’s policies as the clinic does not participate in the practice of therapeutic or elective abortion.

Minimizes harm and maximizes other ethical principles to the extent possible for the client and relevant others:

Autonomy is encouraged by supporting the woman’s decision and getting her a referral to a skilled abortion clinic.

Beneficence is encouraged by making sure the woman is educated on the situation and encouraged to make well informed autonomous decision.

Allows you to operate within the law:

- Justice: Patient cannot be denied access to abortion even when her opinion and beliefs differ from those of the providers.
- Confidentiality: Patient’s information should be kept confidential following HIPAA guidelines. Her records should be handled with caution making sure that her privacy is maintained.
- Consent: Patients require full explanation of the abortion process, benefits, risks, consequences of intervention, consequences of no intervention, as well as alternative interventions in other to give a well informed consent.
PROGRESS NOTE

Kati is a 39 year old very pleasant African American female who came to clinic with complaint of missing her period for 2 months. She reports that had used a home pregnancy test kit which showed that she was pregnant. She came to clinic to confirm her pregnancy and to discuss her options. She is accompanied by her newly wedded husband, Buma. Kati and her new husband did not plan to become pregnant. She is troubled because her husband has sickle cell anemia and she has sickle cell trait. They both had been counseled on the possibility that they have a 50% chance of having a child with sickle cell disease and a 50% chance of having a child with sickle cell trait.

Kati has had 3 children from a previous marriage and Buma (age 25) has had no children and this is his first marriage. They are here to discuss the possibility of prenatal genetic testing. Kati is worried because she would have to choose between having an abortion and possibly taking the risk of raising a child with a genetic disorder. She is open to an abortion if the child is seen to have sickle cell disease but the husband is not sure he would want an abortion because of religious beliefs.

Past medical History
Overweight
Sickle cell trait

Past surgical History
Appendectomy in 1999

Social History
Marital Status: Patient is married. Patient has 3 children (ages 17, 20, and 21). Patient lives with spouse. Spouse has sickle cell anemia.
Patient denies using tobacco.
Patient denies any alcohol use. Patient reports no exposure to high risk behaviors such as sexual behaviors and intravenous drug use.

Family History
Maternal aunt had breast cancer.
Older sister died of sickle cell anemia at age 35; younger brother has sickle cell anemia. Her parents are divorced. There is no other significant family medical history.

Travel History
Patient denies travel outside the United States in past 5 years.

Allergies
No known allergies reported by this patient.

Medications
There are no on-going medications for this patient.
Review of Systems

Constitutional: Patient reports no weight loss, fatigue, loss of appetite, night sweats, fever, or chills.

Skin: Patient reports no skin rash, erythema and other localizing signs and symptoms suggestive of infections.

Lymphatic: Patient reports no lumps in right arm-pits, neck or groin.

Gastrointestinal: Patient reports nausea, no vomiting, no heartburn, no constipation, no diarrhea, and no abdominal pain.

Vitals

Vitals: Height = 68 in, Weight = 174 lb, Temp = 98.1 F, Pulse = 85, Respiration = 18, Systolic BP = 125, Diastolic BP = 84.

Physical Exam

Patient is well developed, well-nourished, anxious looking but in no obvious respiratory distress. Patient appears stated age. There were no pertinent findings on physical exam of this patient.

Assessment:

Lab:

HCG urine – positive pregnancy test

Diagnosis

626.0 ABSENCE OF MENSTRUATION.

Note: Positive pregnancy test. GI symptoms likely related to early pregnancy.

Plan: HCG - URINE, URINALYSIS.

V72.42 PREGNANCY TEST, POSITIVE

Note: Positive pregnancy test.

Plan: PRENATAL VITAMINS OR TABS

Genetic Counseling

OB follow-up in 1 week as needed

Dr Collins W.C MD.
The idea of having an abortion or keeping the pregnancy in a case of a fetus with sickle cell disorder is always associated with some degree of ethical dilemma. Terminating a pregnancy based on a positive sickle cell result is always a difficult decision that involves religious, psychosocial and cultural considerations (Adare, ).

Even with legalization of abortion, the question whether it is right to terminate an innocent life is still a much debated issue (Adare, ). One of the debated questions are:

- Is the fetus a person with moral and legal rights (Lo, p.)?
- When does personhood begin: at conception, viability, birth, or some other time (Lo, p.)?
- Do women have an ethical right of reproductive liberty that encompasses a right to abortion (Lo, p.)?
- Even in cases where the decision is made to keep the pregnancy the question of whether it is right to bring a child to a world of suffering, agony, and untimely death, remains a dilemma.

Other ethical dilemmas are:

- Should a health provider be forced to care for a woman undergoing abortion even when it is contrary to their beliefs?
- Can a spouse of a pregnant woman force her to have a baby when she wants to have an abortion?