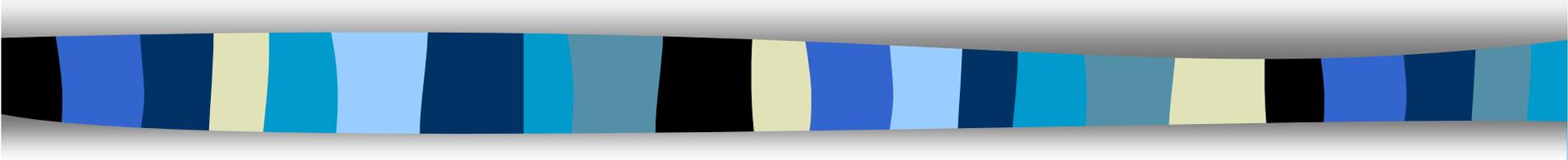


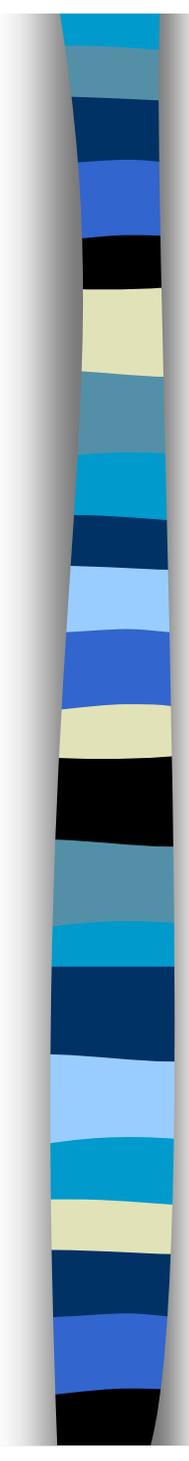
# Genetic counseling issues in metabolic disorders



Jennifer L. Sloan PhD, MS

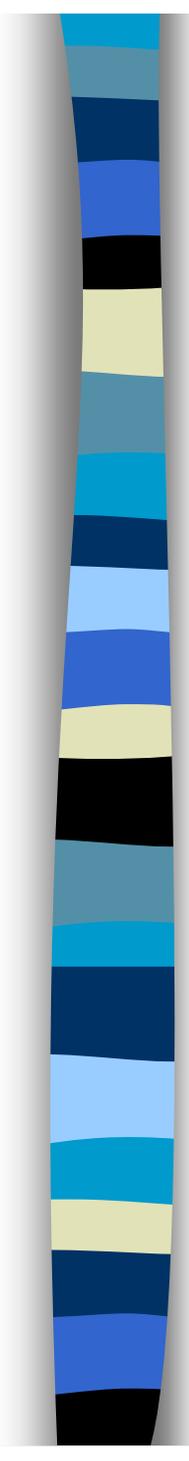
FOD/OAA meeting

June 23, 2006



# Genetic counseling & metabolic disorders

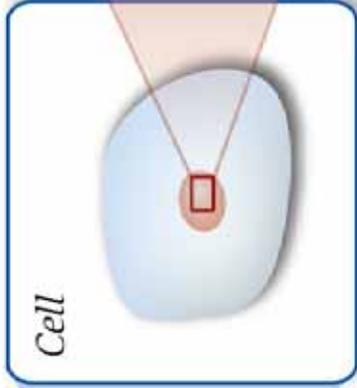
- Education about genetics
  - Diagnosis and treatment
  - Risks to other family members
  - Genetic testing for family members (prenatal diagnosis, carrier testing)
- Counseling: psychosocial impact of the disorder on the family
  - Affected children
  - Parents
  - Well siblings



# Genetic counseling & metabolic disorders

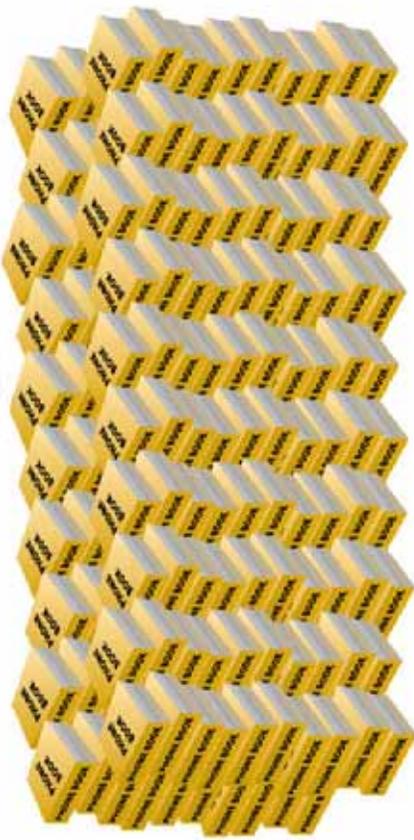
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  - **Parents**
  - **Well siblings**

# The human genome contains about 3 billion nucleotides



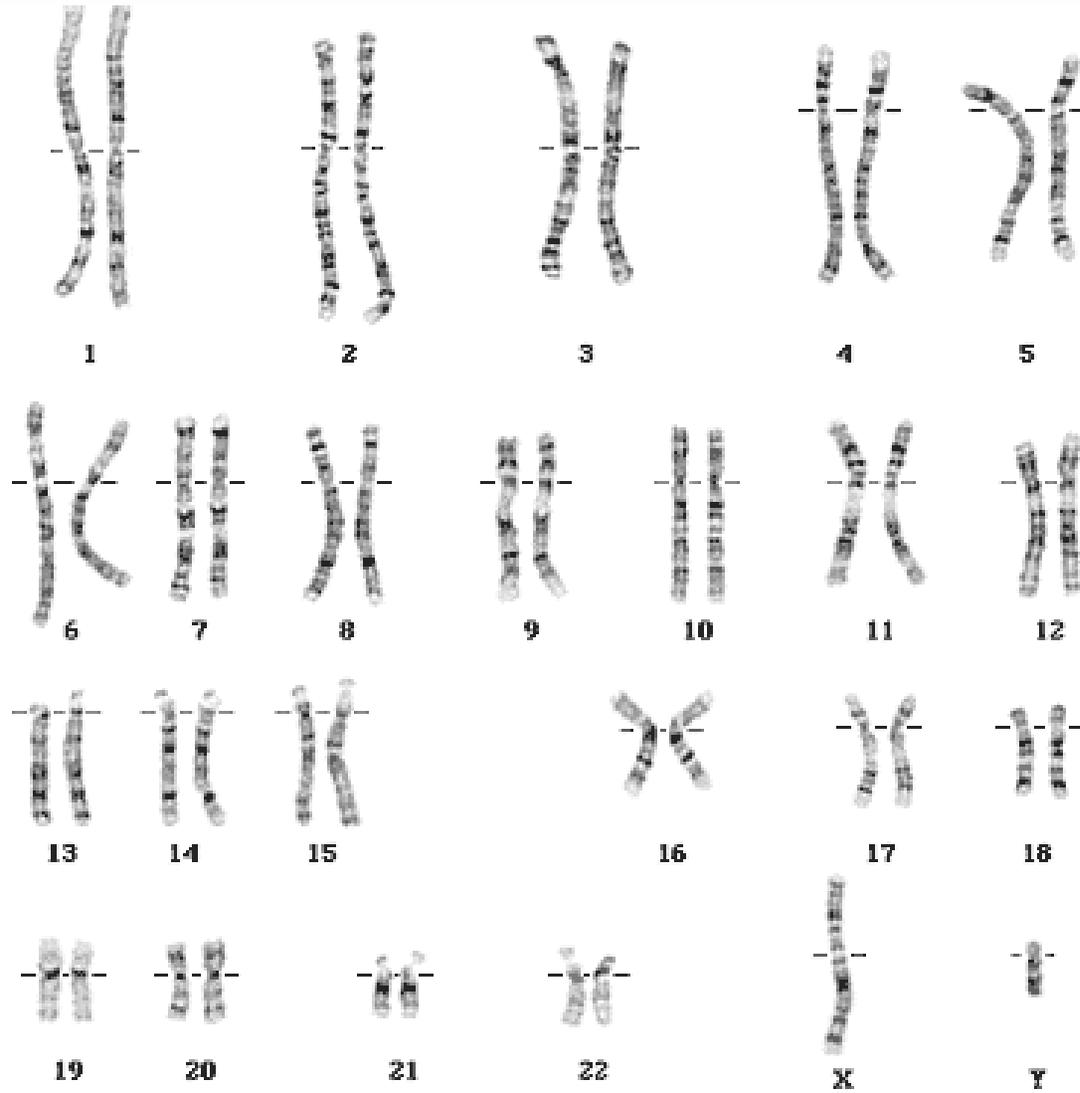
...AGGTTCAGGCCATCAGATTCCGCAATCGCCTTG  
AGCAATCGCTTGCAGATACGAAAGCTTATACC  
TATGTCCTAGGTCAGTGTTCAAAAGTTTGT  
TCCATAAAAGTAAACATTTGTGCTGCAGGATTT  
CTCAGACGGACCAGTTTGCTAAAGTACTCCGG  
GTGCTCCACAAGCTTACATAGAATGTGAAG  
CTTACAAAACATCATCAGACACAGAGAACATCTC  
CTGGACTGAGTTTAAACACAATTGGAAA...

3 billion nucleotides would fill  
about 200 1,000-page phone books



National Human Genome Research Institute

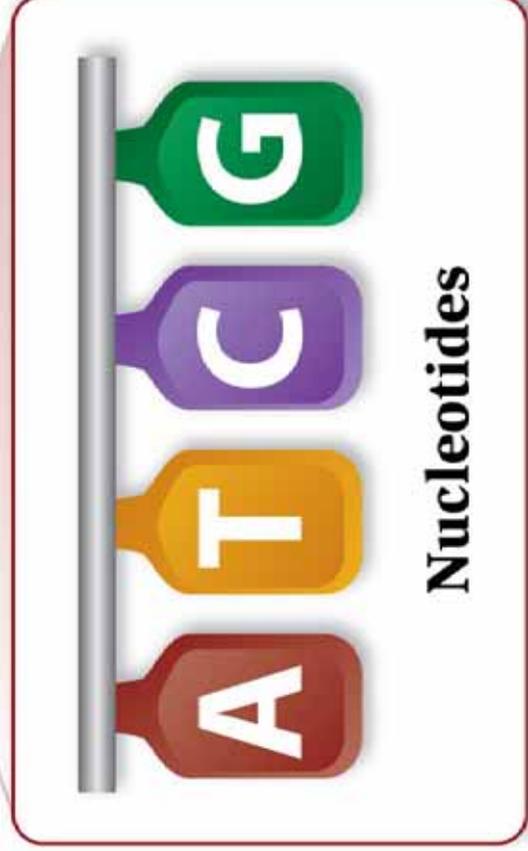
# There are 23 pairs of human chromosomes



The building blocks of DNA are arranged into very long strands

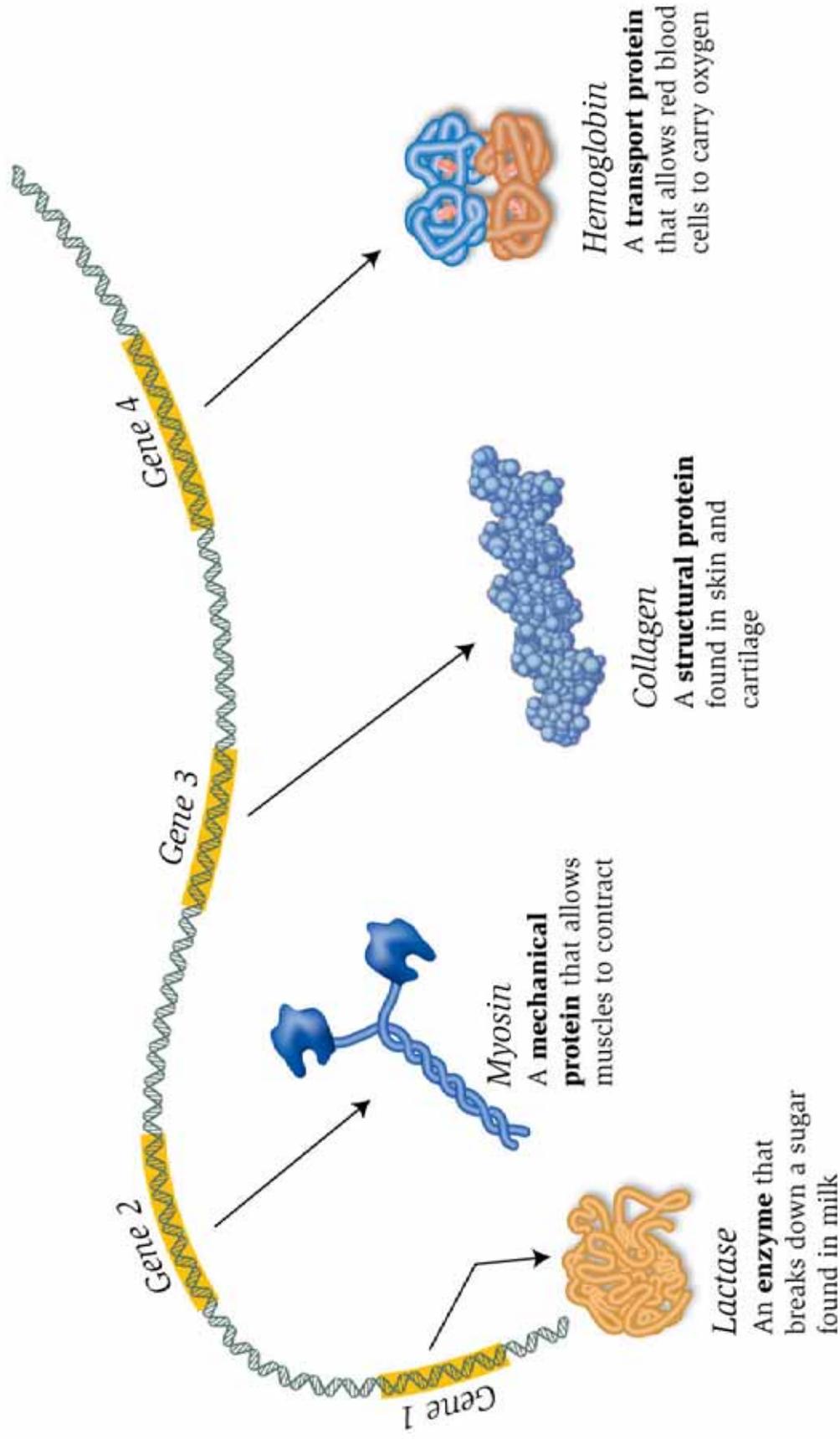
Strand of DNA

A G G T T C A G G C A T C A G A T T C G C A A T C G C T T G A G C A A T C G C A T A C G A



National Human Genome Research Institute

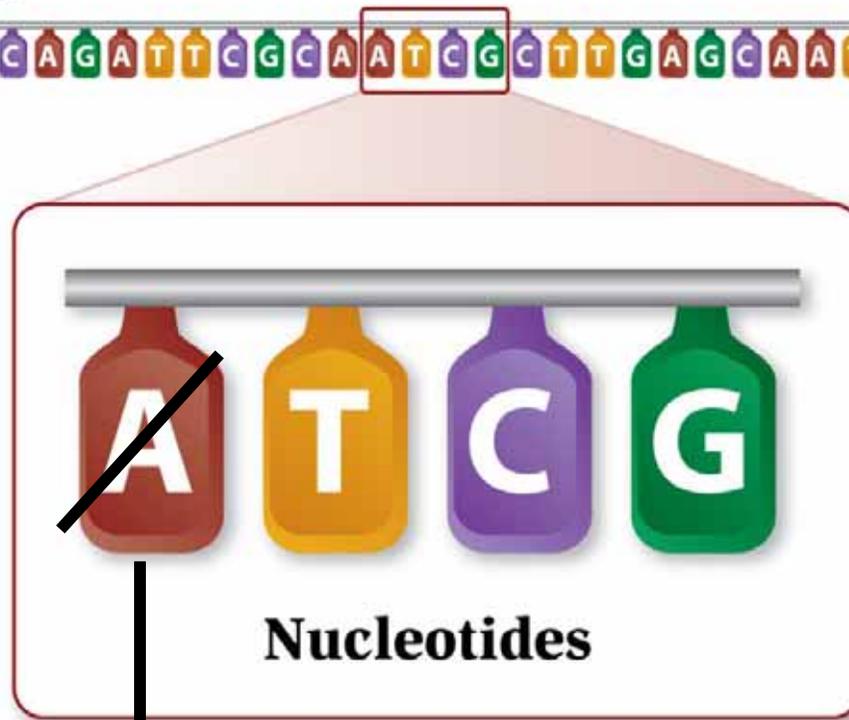
# Each protein carries out a unique function



National Human Genome Research Institute

# The building blocks of DNA are arranged into very long strands

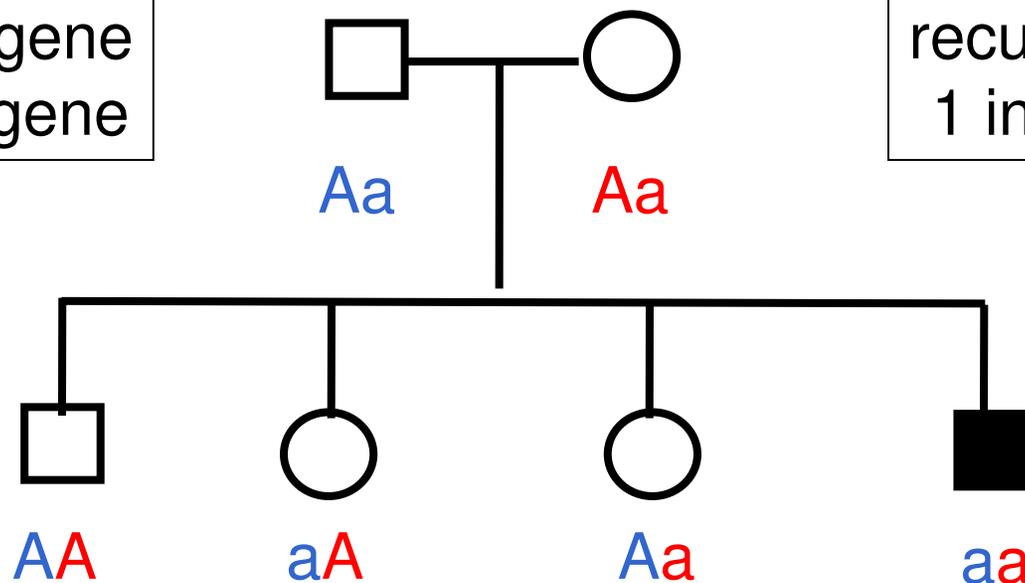
Strand of DNA



# Most metabolic disorders follow autosomal recessive inheritance

- Two copies of every gene
- Both copies are altered
- Typically no family history
- We all carry 5-10 recessive genes!

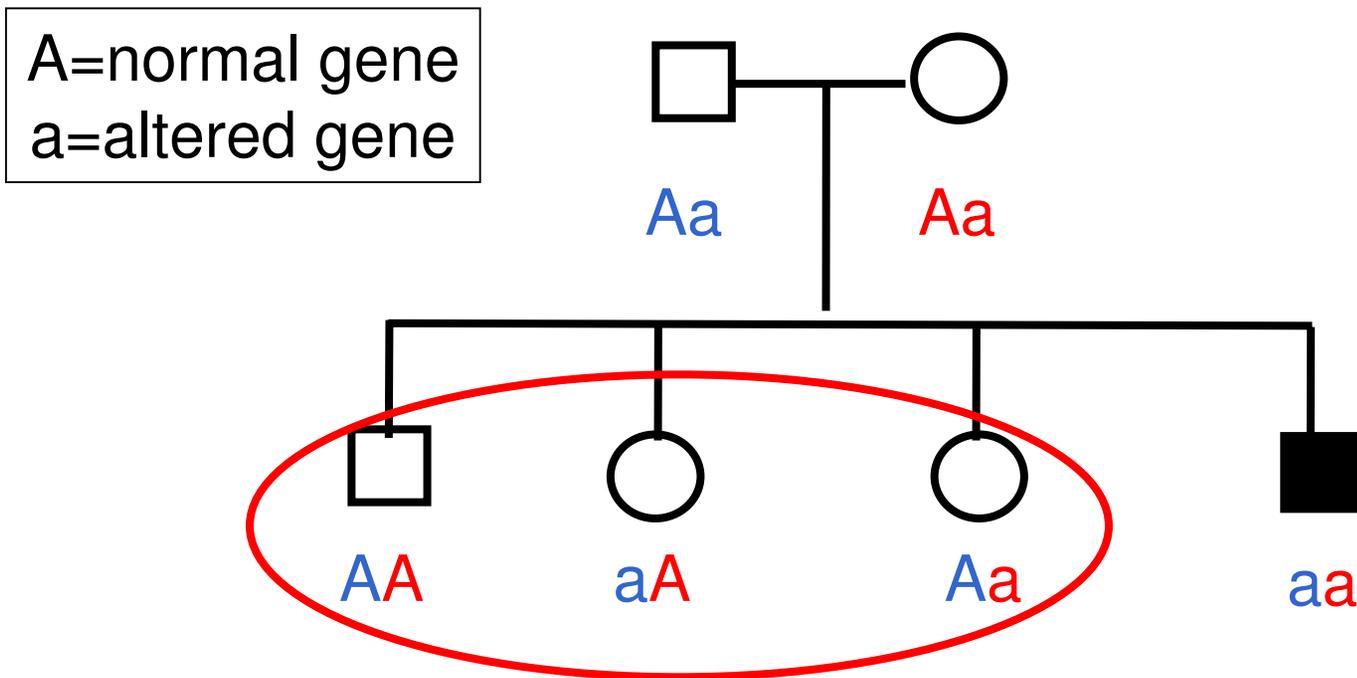
A=normal gene  
a=altered gene

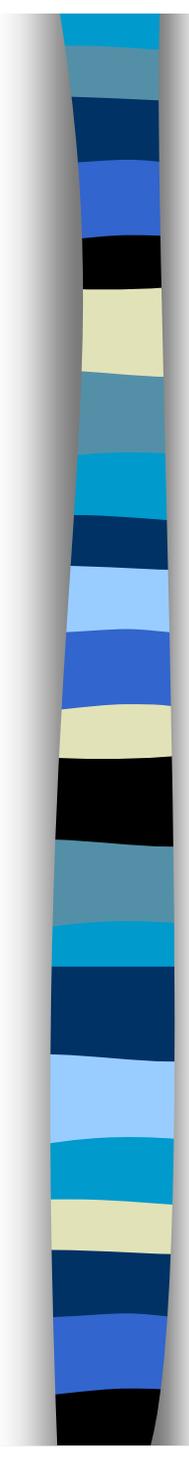


recurrence risk  
1 in 4 or 25%

# What are the chances my other children are carriers?

- 2/3 or 66% chance that an unaffected sibling is a carrier

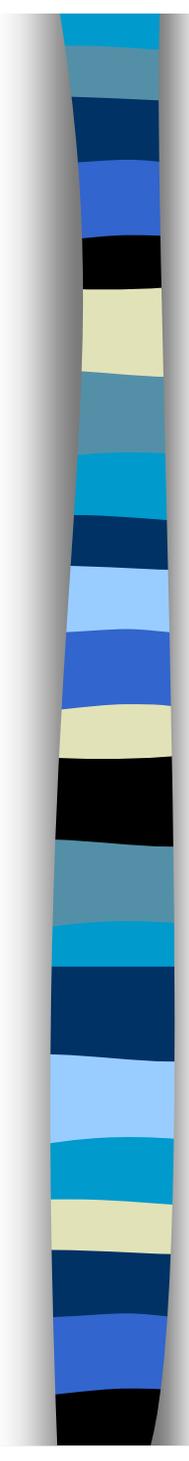




## What are the chances my grandchildren will be affected?

Chance sib is a carrier	Chance partner is carrier (depends on how common)	Chance both pass on altered gene	Chance each grandchild affected
2/3	1/50 1/100	$1/2 \times 1/2$	1/300 or 0.33% 1/600 or 0.17%

- Both parents must be carriers for child to be affected
- 99.5 % chance (or greater) that child will not be affected

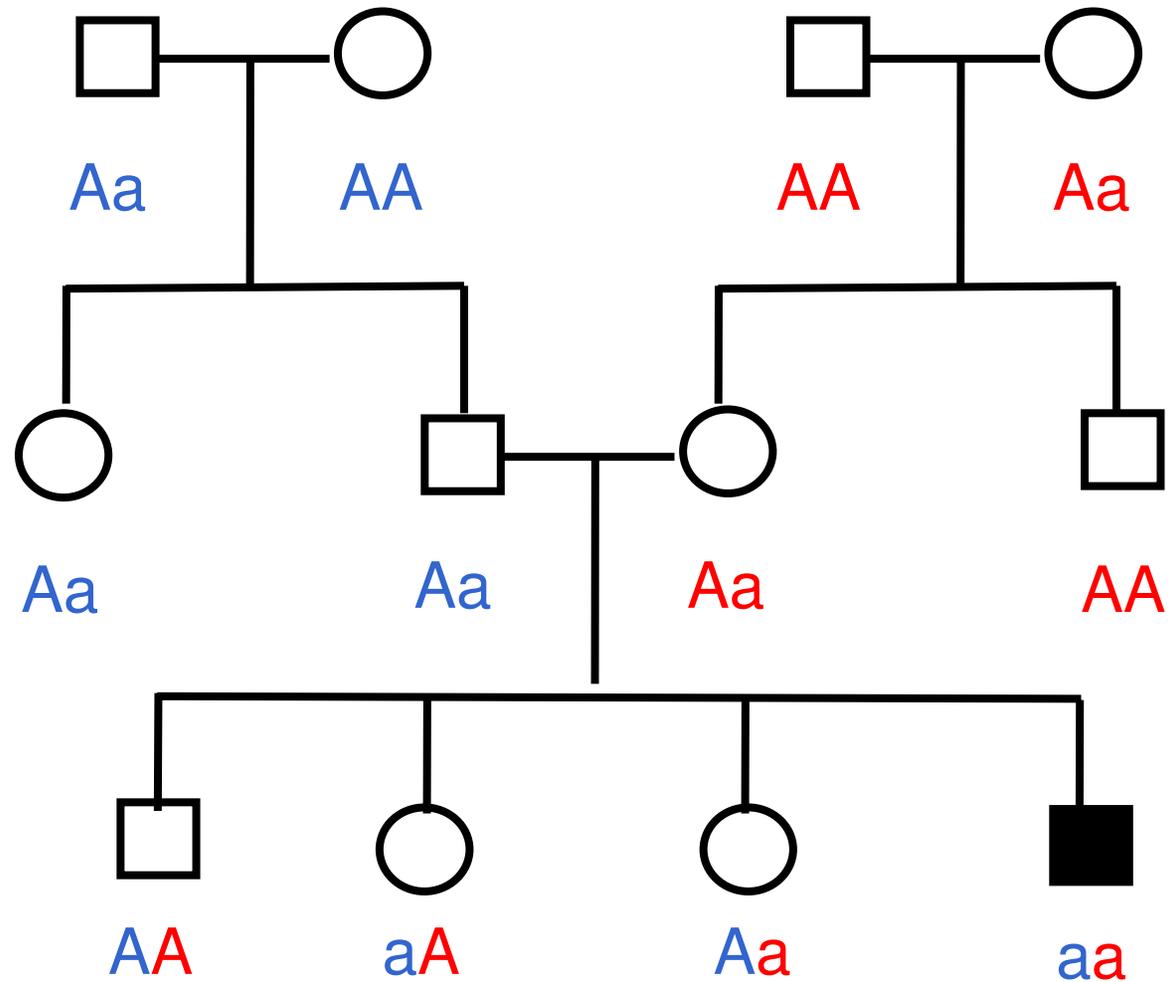


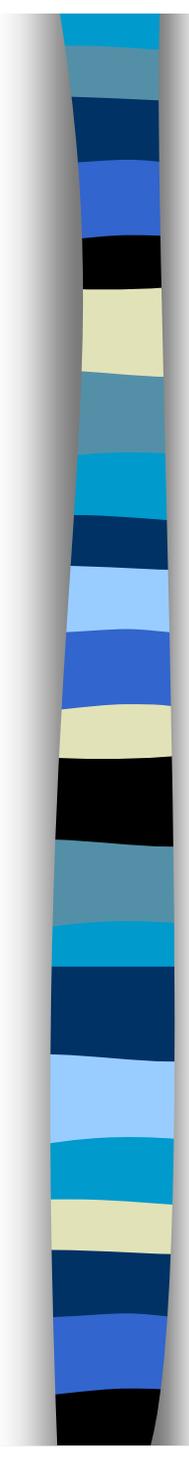
## What are the chances my grandchildren will be affected?

Chance affected person is a carrier (aa)	Chance partner is carrier (depends on how common)	Chance both pass on altered gene	Chance each grandchild affected
1/1	1/50 1/100	$1/2 \times 1/1$	1/100 or 1.0% 1/200 or 0.5%

- Both parents must be carriers for child to be affected
- 99% (or greater) chance that child will not be affected

What about the other family members?

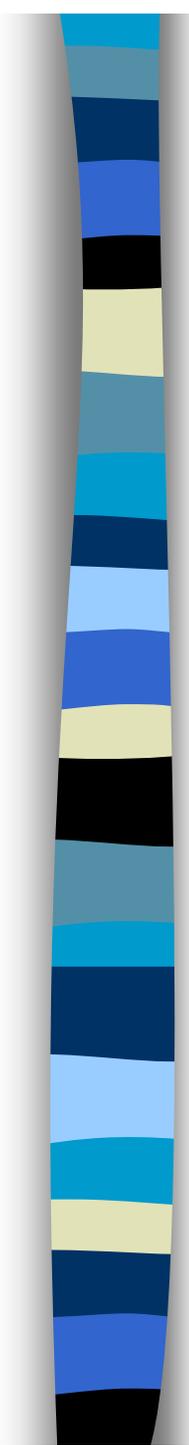




# Nieces and nephews?

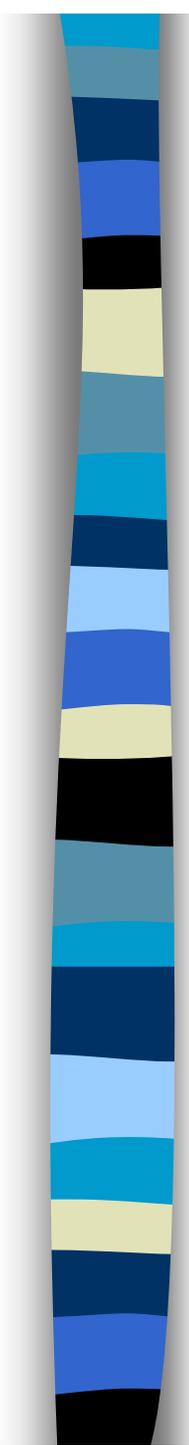
Chance sib is a carrier	Chance partner is carrier (depends on how common)	Chance both pass on altered gene	Chance each grandchild affected
1/2	1/50 1/100	$1/2 \times 1/2$	1/400 or 0.25% 1/800 or 0.0125%

- Both parents must be carriers for child to be affected
- 99.75% (or greater) chance that child will not be affected



# Genetic counseling & metabolic disorders

- Education about genetics
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  - **Parents**
  - **Well siblings**



## Impact of metabolic disorder on parents

- Initial diagnosis of chronic illness
  - loss of the perfect child
  - Feelings of grief, fear, anger, sadness, guilt
- Very little information on how metabolic disorders affect families

# Psychosocial issues and coping strategies in families affected by urea cycle disorders

Julie A. Cederbaum, BA, Cynthia LeMons, Mindy Rosen, BA, Mary Ahrens, MS, Sharon Vonachen, BSN, and Stephen D. Cederbaum, MD

THE JOURNAL OF PEDIATRICS  
JANUARY 2001

- 30 item survey of urea cycle disorder parents about stressors in family
- 118/293 responded (40% response rate)

Table I. Description of the survey sample responders

Geographic distribution of respondents	
East	30
Southeast	16
Midwest	31
Southwest	8
West	22
Sex of respondents	
Male	24%
Female	76%
Age	
Mean age of parents (y)	42.6 (normal distribution)
Mean age at diagnosis (mo)	24.8
Diagnosis of proband	
OTC deficiency	53.2%
ASS deficiency	15%
ASL deficiency	15%
CPS deficiency	10%
Arginase deficiency	2%
Location of probands	
Living at home	79% (remainder are deceased, living on their own at school, or institutionalized)
Siblings in the home	
Yes	77%
No	23%

OTC, Ornithine transcarbamylase; ASS, argininosuccinate synthetase; ASL, argininosuccinate lyase; CPS, carbamyl phosphate synthetase.

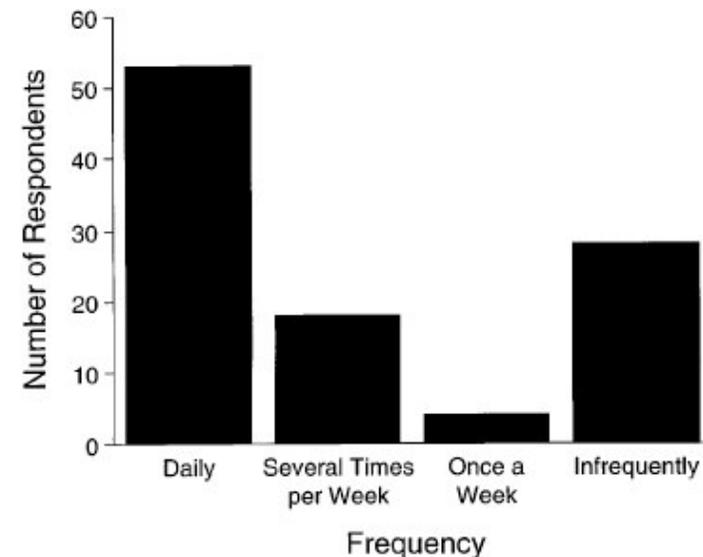
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**Table II.** Responses to the question, "What was your initial reaction to hearing your child's diagnosis?"

Fear	72%
Anger	22.5%
Guilt	26%
Disappointment	24%
Concern	64%
Relief	29%
Sadness	54%



**Fig 2.** Frequency distribution of responses to question of how often respondents think of possibility of death of their child.

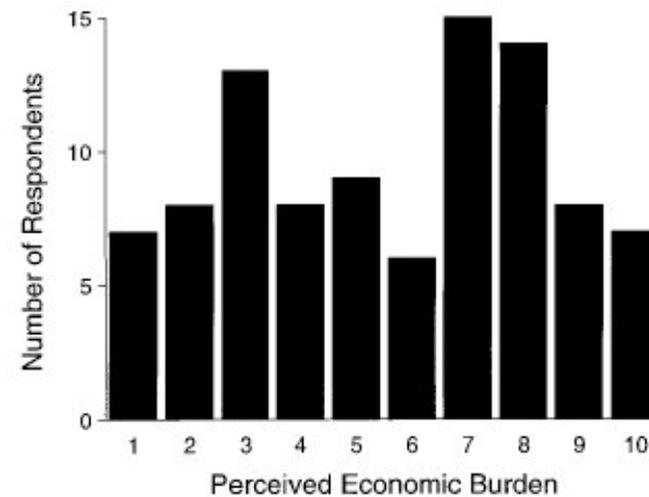
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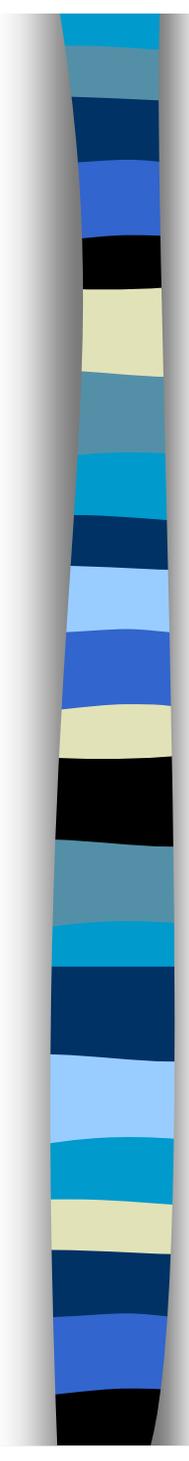
THE JOURNAL OF PEDIATRICS  
JANUARY 2001

*Table III.* Responses to the question, "What stressors has having a child with a metabolic disorder placed on your life?"

Financial	49%
Loss of friends	19%
Emotional	92%
Mental	48.5%
Interpersonal	36%
Lack of freedom	54%



*Fig 3.* Frequency distribution of perceived financial burden, on scale of 1 to 10, on family of having child with urea cycle defect.



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**Table IV.** Responses to the question, "How has having a child with a metabolic disorder changes your daily activities?"

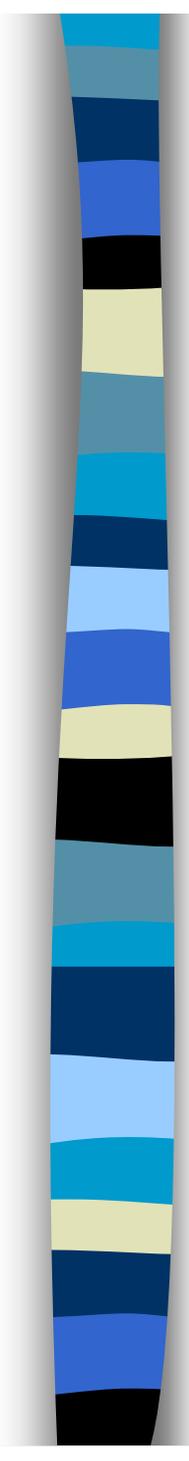
Less socializing	42.5%
Less personal time	66%
Less time for other children	43.5%
More time for my children	11%

---

**Table V.** Responses to the question, "How has having a child with a metabolic disorder affected your career decisions?"

Had no effect	33%
Feel as though I cannot change because of insurance	24%
Chose less demanding job	15.5%
No longer work outside the home	26.2%

---



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*Table VI.* Responses to the question, "In what ways has having a child with a metabolic disorder had a positive effect on you?"

More compassionate	63%
Made me an activist	25%
Taught me my strengths	67.5%
Made me more patient	49.5%
Awakened my world view	42%

*Table VII.* Responses to the question, "In what ways has having a child with a metabolic disorder affected your relationship with your partner?"

Brought us closer together	50%
Made us better communicators	27%
Caused conflict	46%
Caused us to separate	9.5%
No substantial effect	91%

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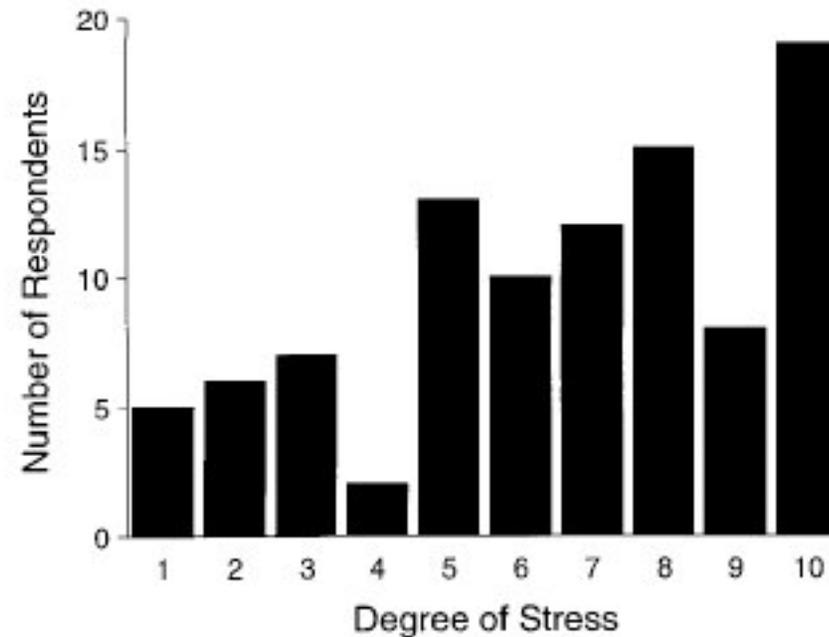
**Table X.** Responses to the question, "Where does your psychologic and social support come from?"

Spouse	71.5%
Family	73%
Children	26.5%
Religion	36%
Other parents/support group	23%
Friends	32%

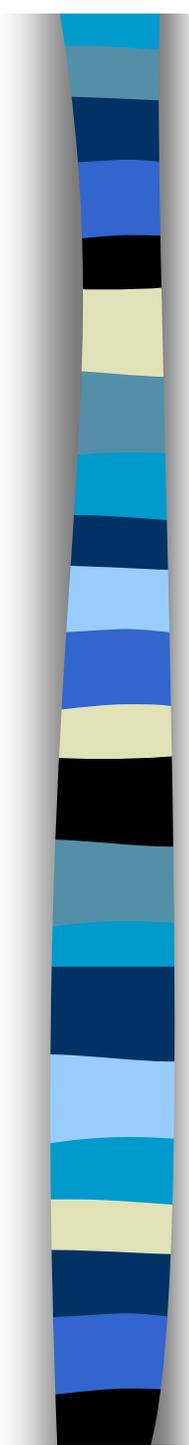
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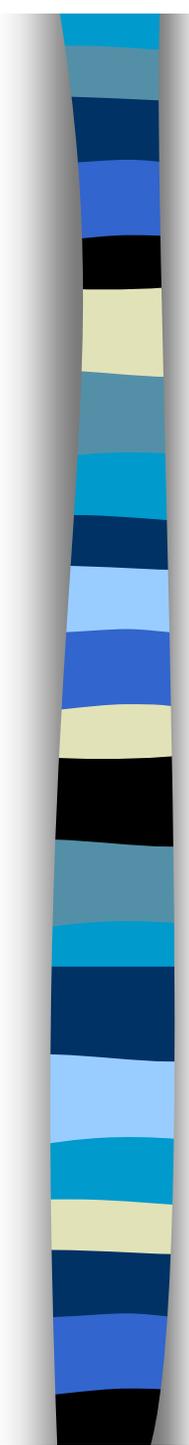


**Fig 5.** Frequency distribution, on scale of 1 to 10, of perceived degree of stress, related to medication and its side effects, in families with child with urea cycle defect.



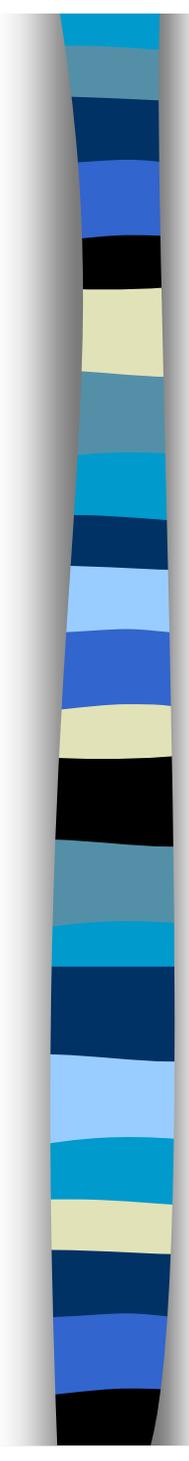
# Summary

- Parents of children UCD report negative and positive impact of the disorder
- Worry about mortality, financial issues, changed daily life and relationships, stress of management
- Identified strengths, more compassionate, brought spouses closer together



# The well sibling

- ~18% of children in US have chronic medical condition
- Well sibs at risk for immediate and long-term emotional, behavioral, physical and psychosocial consequences
- Sibling issues infrequently addressed
- Medical profession focuses on the ill child
- Family interventions often focus on parents
- Psychiatrists and psychologists usually only consulted when situation becomes serious (behavior problems etc)



## Amber Catford-Robinson, 5

My sister's name is Naomi and my name is Amber. I am five and she is three. We think Naomi has Rett syndrome and some other things.

I like to play with Naomi. If she cries, I can make her laugh by laughing! Naomi has an electric piano. Sometimes I move her arms and help her push the keys to make music. I love to play with her. She loves me best of all.

Naomi has a g-tube. A g-tube is a tube that goes into her tummy so she can drink a special kind of formula. Naomi throws up a lot, and I don't like it when she throws up. When my parents are dealing with her, I'm alone and nobody pays attention to me. It's like I'm not even there. If she did not have this sickness, I would like it much better.

Last year I went to Camp Me and My Family and met some new friends who have sisters and brothers with special needs. We had a lot of fun! One girl had a brother who has a g-tube and was in a wheelchair and couldn't talk, just like Naomi.

If Naomi didn't have special needs, I would be much happier. Thinking of all the things we could do together fills up my brain with thoughts! We would do all sorts of things—play ball, make up games together, or play in the hot tub.

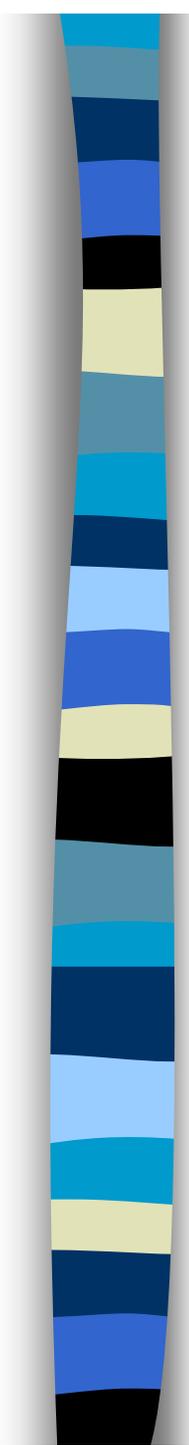
When we go to school, I sometimes like to bring Naomi into my classroom and introduce her to my classmates. Sometimes, if we are early enough, I go into her classroom and see her classmates.

I worry about Naomi sometimes. When she is in school I wonder what she is doing and if she is having a good day. When I get home from school, I can't wait to see the art she did at school.

On weekends I like friends to come over to play and meet Naomi.

I wish she will get better sometime in her life. But I do not wish she will get better in days, weeks, months, or years. I just wish she would get better the minute I wish it.

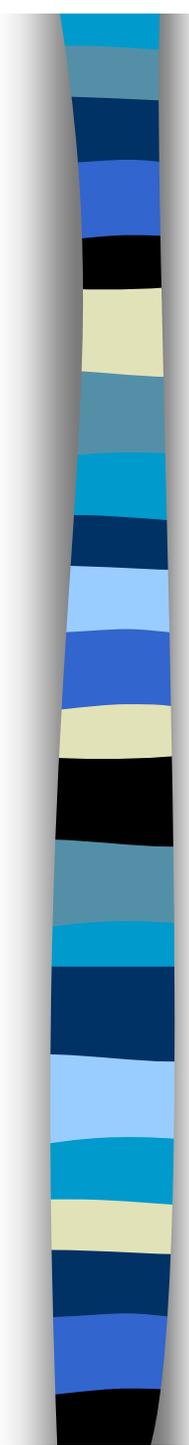
—Meyer, D.J. *Views from our shoes: growing up with a brother or sister with special needs*



# Themes of stress

- Responsibility
- Loneliness/Resentment
- Fear
- Jealousy
- Guilt (survival guilt)
- Sadness
- Embarrassment
- Confusion

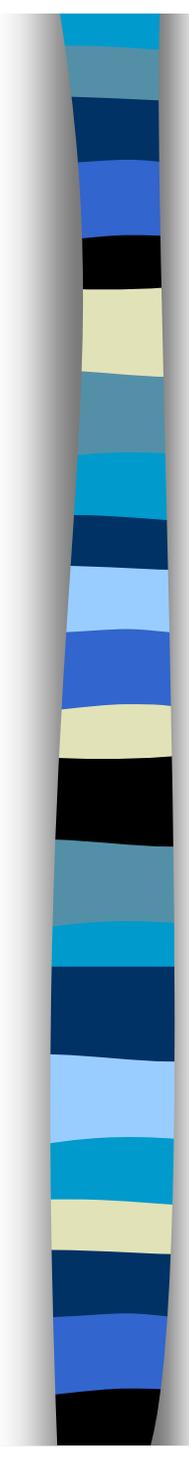
Fleitas, J. When Jack fell down...Jill came tumbling after: siblings in the web of illness and disability. *Am J Mat Child Nursing* 25(5):267-273, 2000.



# Themes of resilience

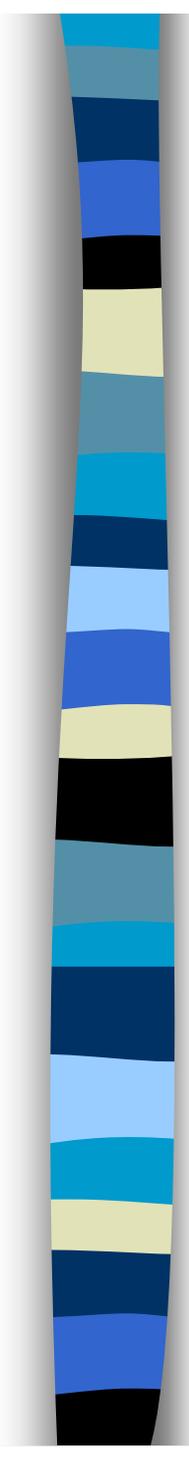
- Life lessons
- Independence
- Altruism

Fleitas, J. When Jack fell down...Jill came tumbling after: siblings in the web of illness and disability. *Am J Mat Child Nursing* 25(5):267-273, 2000.



# What can parents do?

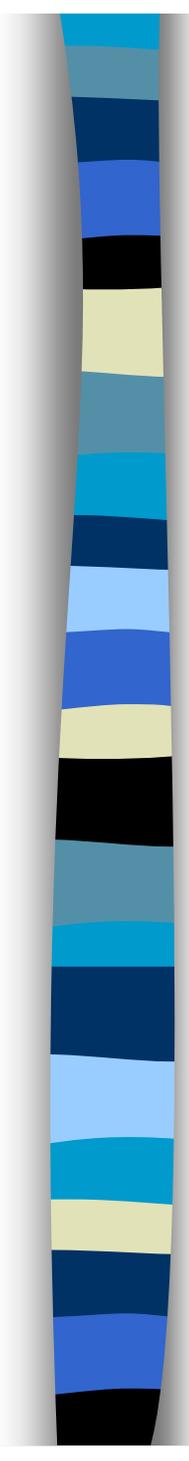
- Right to own life
- Acknowledge concerns
- Realistic expectations
- Expect typical behavior for well sibs (fights etc)
- Have high expectations for affected child
- Concern for future
- Include both daughters and sons
- Celebrate well child's achievements and milestones
- Parent's perspective on disability important
- Consider including well sib in clinic visits, IEP meetings



# What can parents do?

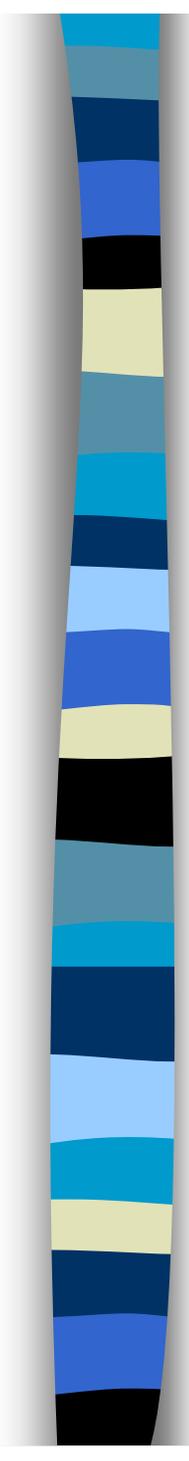
- Open communication
- Learn more about sibling experiences
- Give age-appropriate information
- Plan for future of special needs child
- Opportunities to meet other siblings of children with special needs
- Designate time for well sibs

Meyer, D.J. and Vadasy, P.F. Sibshops: Workshops for brothers and sisters of children with special needs. 1994.



# Resources: Sibshops

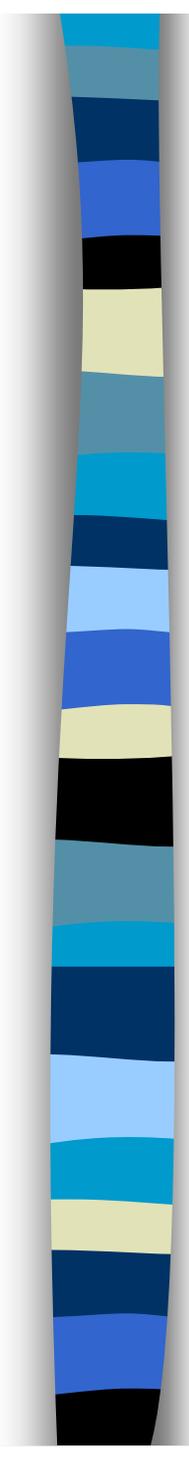
- Groups where sibs can go for support, networking, fun
- Books
  - Meyer, D.J. and Vadasy, P.F. Living with a brother or sister with special needs: a book for sibs
  - Meyer, D.J. Views from our shoes: growing up with a brother or sister with special needs
  - Meyer, D.J. The Sibling Slam Book: What it is *really* like to have a brother or sister with special needs
  - Many others
- SibKids and SibNet listservs
- [www.thearc.org/siblingsupport](http://www.thearc.org/siblingsupport)



# Resources: Sibling Center

- Intervention 4 sessions with therapist
  - Visit 1 and 4 parents involved
- Identify ways to improve family communication
- Positive results
  - less angry acting out sibling behavior
  - improved family communication
  - gratitude for help given

Fanos, J.H. et al. The sibling center: a pilot program for siblings of children and adolescents with a serious medical condition. *J Pediatr* 2005.



# Summary

- Metabolic disorders can have dramatic impact on all family members
- Seek support when appropriate
- More research is needed