Collecting and Using Family History In Assessing Risk

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May 14,2009

Objectives?

- Why family history is important to you and your patients
- How to take and interpret a family history
- The various new tools available for compiling a family history
- What to do with this information

Personalized Medicine

An accurate family history including family pedigree remains the fundamental tool to use in designing an individualized management and treatment plan for patients

The Family History

The American Medical Association has stated that the family tree has become the most important genetic test of all and is the first line of action

Family History

- Can improve patient care by:
  - Early ID of increased risk for chronic diseases or cancer and can often improve, delay or even prevent adverse outcomes
  - Reveals patterns of inheritance
    - Information for other family members
  - Provides information to help make decisions about reproduction

Desirable Features in a Family History Tool

- Self-administered (information gathering)
- Simple (simplicity varies)
- Adaptable
- Interprets risk (+/-)
- May be useful for targeting interventions
- Ideally, tied to resources for risk-appropriate prevention (medical, community)

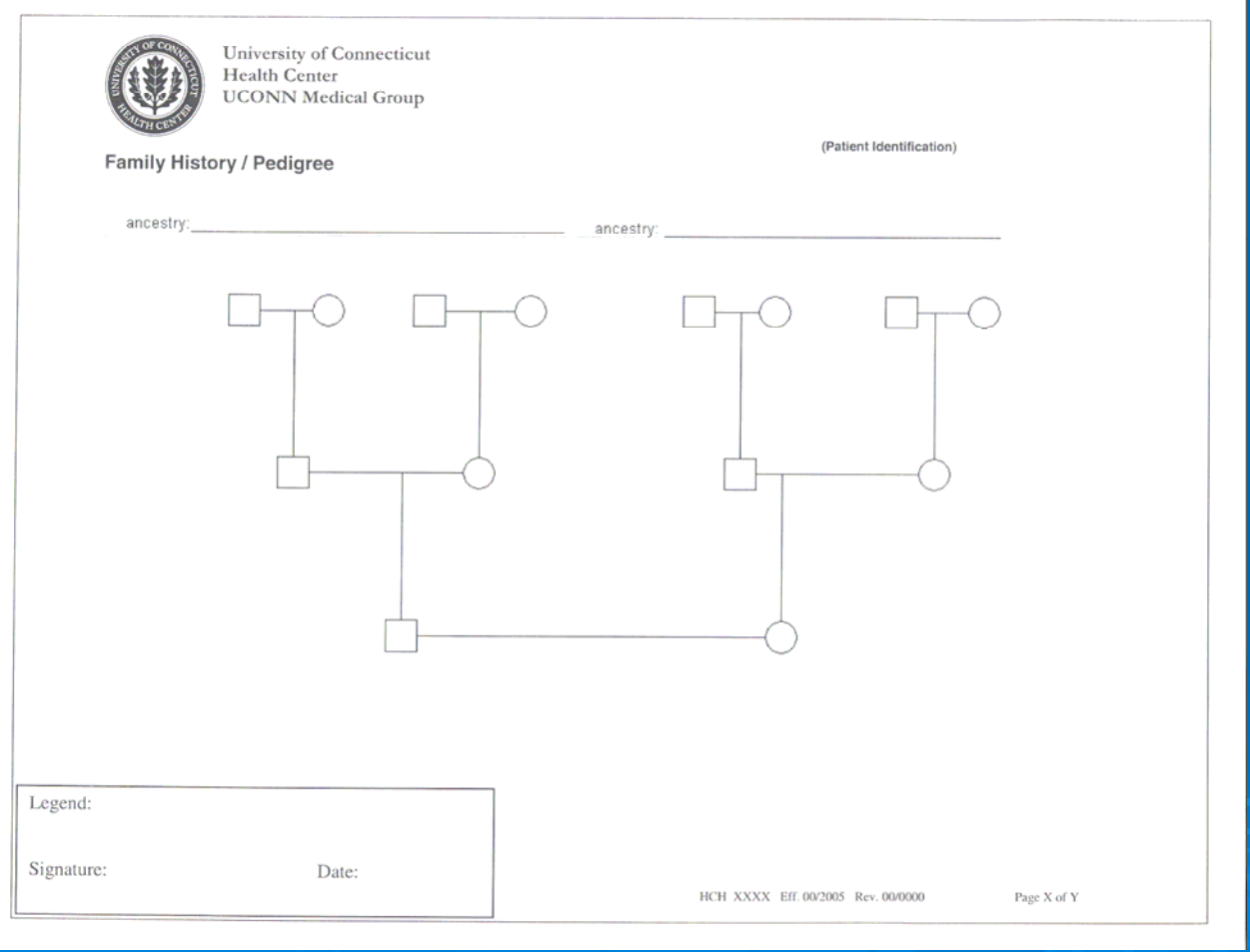
The Family Pedigree

- Three to four generations
  - First, second and ideally third degree relatives
  - Used standardized pedigree symbols
  - Gather information bout both paternal and maternal lineages
  - Include information about ancestry/ethnicity
  - Document pertinent information about the individuals with the condition in question
  - Include original country of origin

Constructing a Pedigree

- The “patient” (proband, propositus, index case)
- Children
- Siblings
  - Nieces and nephews
- Parents
- Grandparents on each side at a time. Include:
- Aunts and uncles
  - Cousins

How to Take a Family History



University of Connecticut
Health Center
UCONN Medical Group

(Patient Identification)

Family History / Pedigree

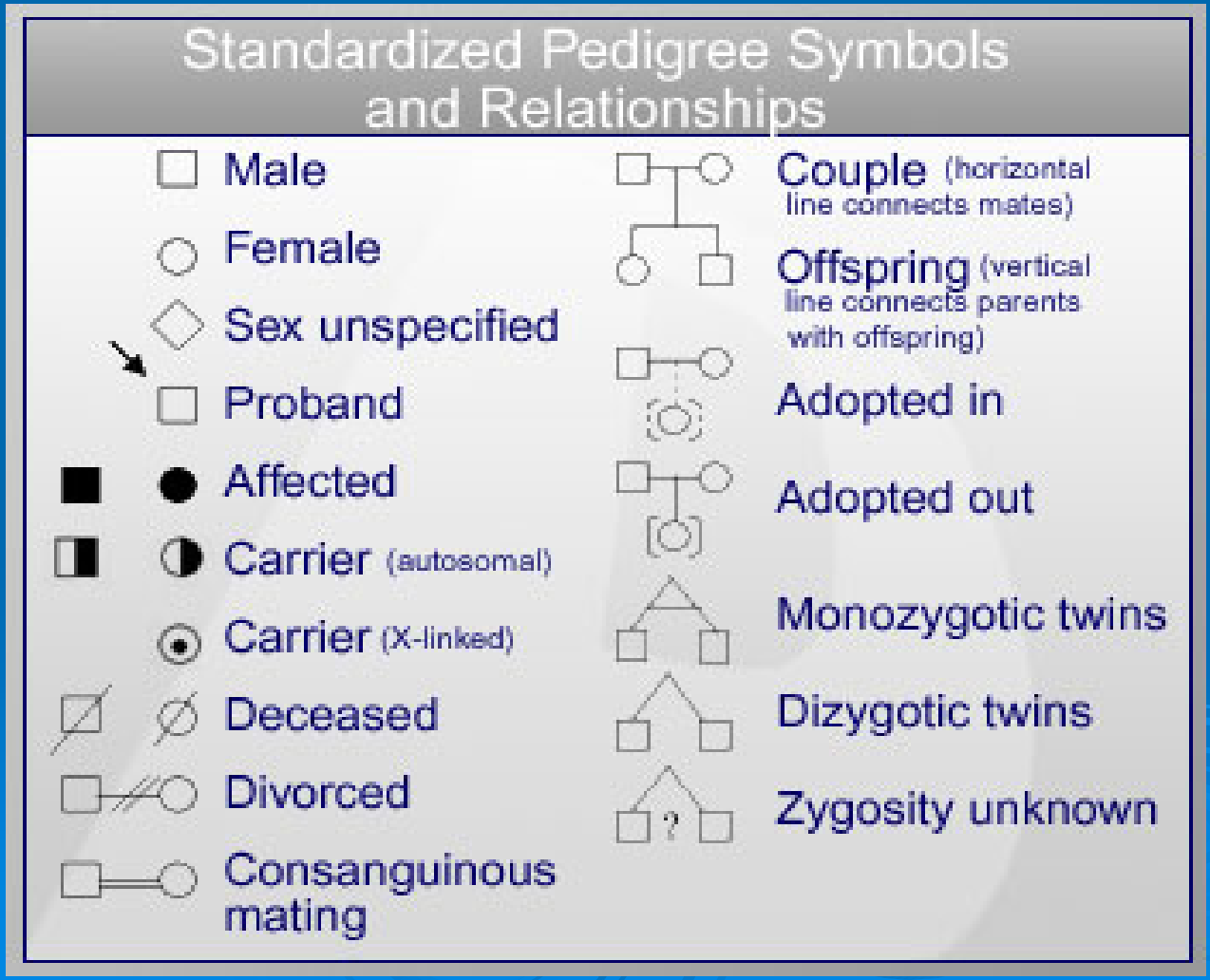
ancestry:_____ ancestry: _____

Legend:

Signature: Date:

HCH XXXX Eff. 00/2005 Rev. 00/0000 Page X of Y

The Family Pedigree: A tool to graphically organize important family medical information and relationships

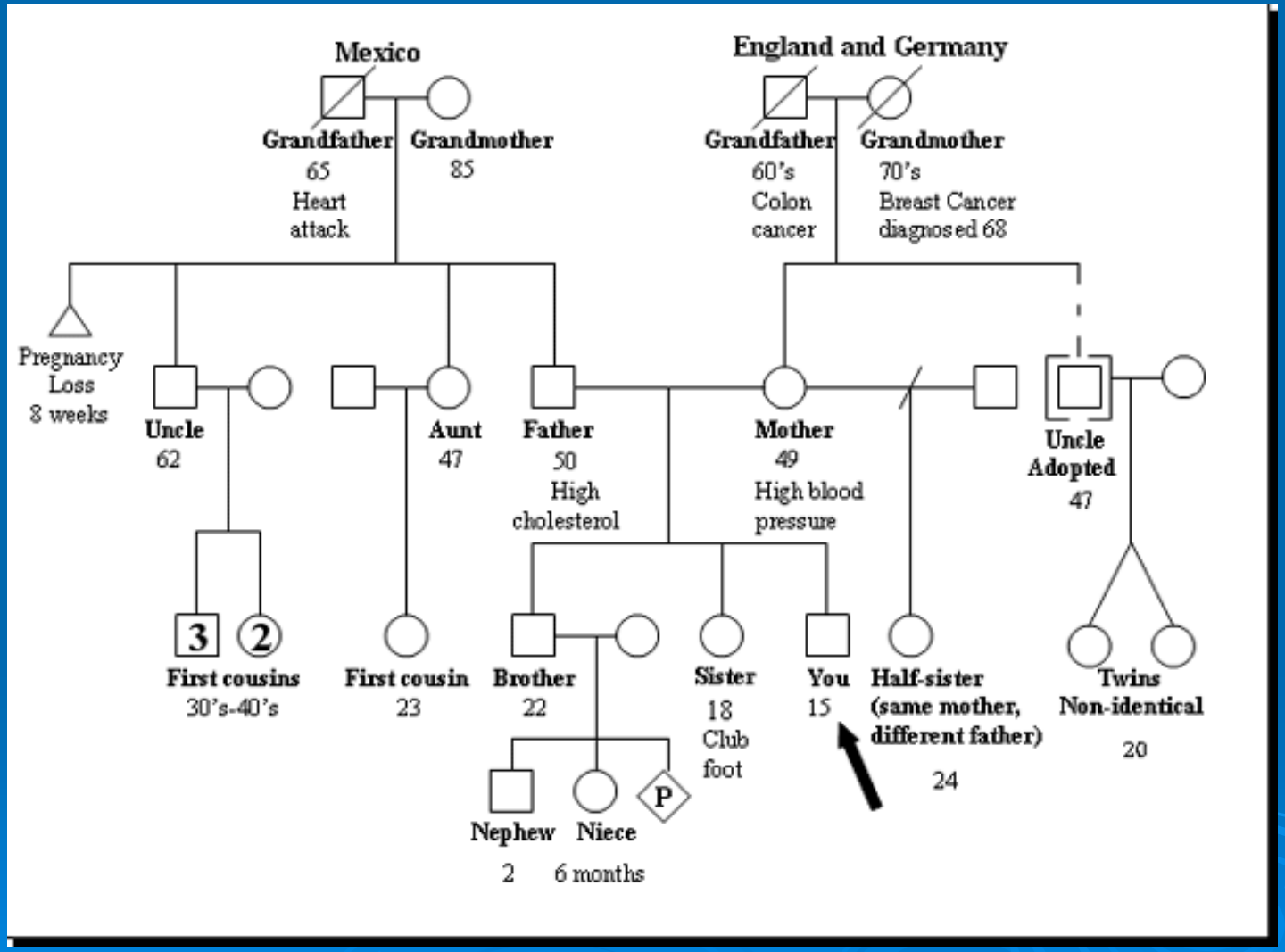


Constructing a Pedigree

- Age or date of birth
- Medical problems such as:
  - Cancer
  - Heart disease
  - Diabetes
  - Asthma
  - Mental illness
  - And features of possible syndromes (in a more high-risk context)

Constructing a Pedigree

- Note the ages at which the conditions occurred
- Birth defects such as spina bifida, cleft lip, heart defects, others
- Learning problems, mental retardation
- Vision loss/hearing loss at a young age
- For family members with known medical problems, record if they smoked, their diet and exercise habits, and if they were overweight


Mexico
Grandfather
65
Heart
attack
Grandmother
85
England and Germany
Grandfather
60's
Colon
cancer
Grandmother
70's
Breast Cancer
diagnosed 68
Pregnancy
Loss
8 weeks
Uncle
62
Aunt
47
Father
50
High
cholesterol
Mother
49
High blood
pressure
Uncle
Adopted
47
3
2
First cousins
30's-40's
First cousin
23
Brother
22
Sister
18
Club
foot
You
15
Half-sister
(same mother,
different father)
24
Twins
Non-identical
20
P
Nephew
2
Niece
6 months

Possible Interventions

- Earlier and more frequent screening
- Education about symptoms
- Preconception or prenatal informed decision-making
- Prophylactic surgery
- Environmental/lifestyle changes:
  - Take or avoid certain medications
  - Lifestyle changes (diet, exercise, habits)

Case #1:

- Michael, a 16-year-old male, comes to you for evaluation of two episodes of "nearly fainting" in the last week while playing football. Michael has been on the varsity team for two years. His past medical history is unremarkable.
- A systems review reveals no obvious cause for his near syncope. However, you detect a systolic murmur at the left sternal border. A stat electrocardiogram shows ventricular hypertrophy, deep Q waves and cardiac ischemia.

Case #1 Continued:

A subsequent echocardiogram shows a septum measuring 17 mm, consistent with a diagnosis of hypertrophic cardiomyopathy (prevalence 2 per 1000 in young adults.)

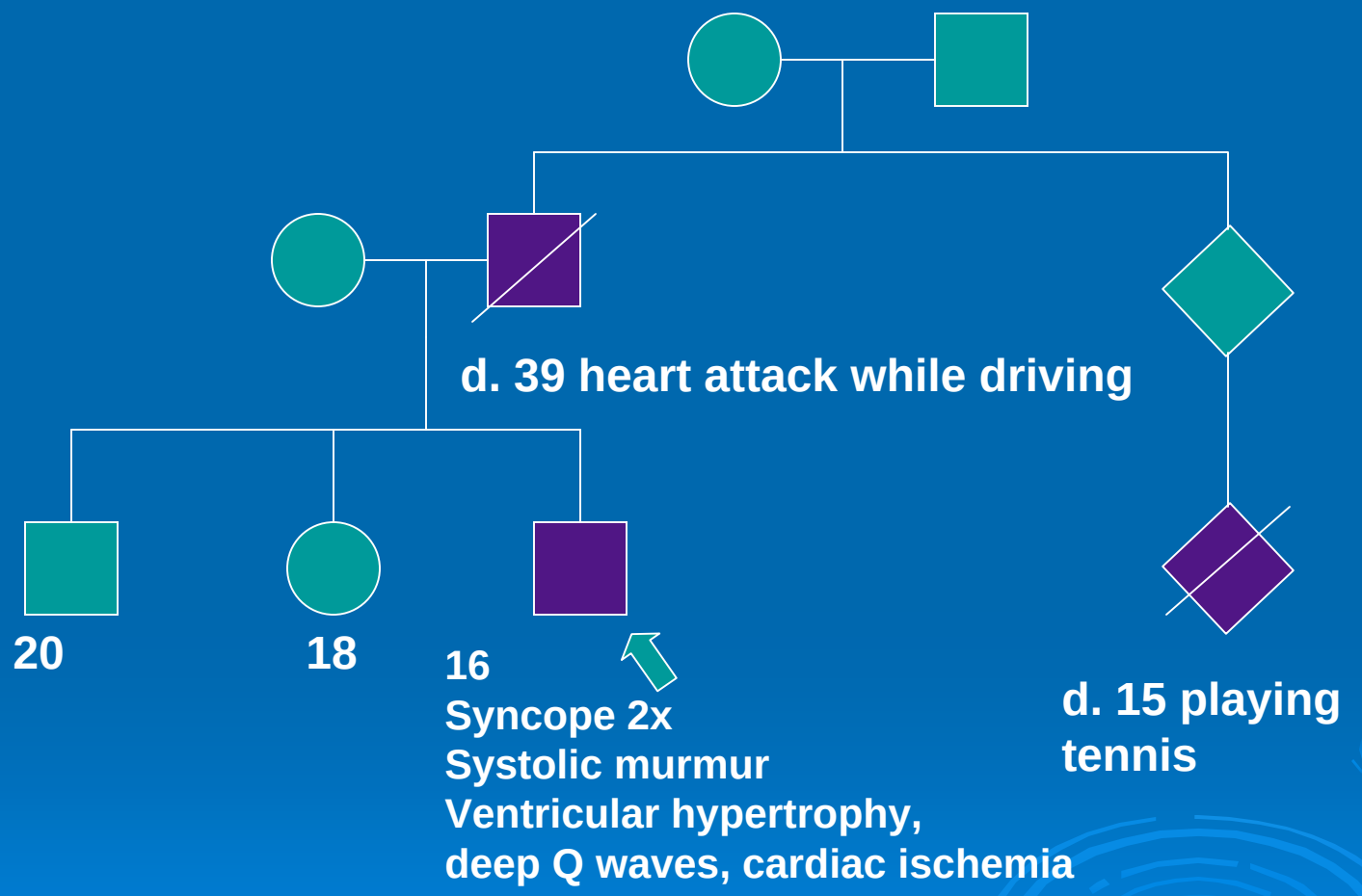
Q. How could family history help you treat this patient?

Case from March of Dimes, source re: hypertropic cardiomyopathy
Maron, BJ et al. Circulation. 1995 Aug 15;92(4):785-9

Case #1 Outcome:

A. In reviewing the extended family history, you learn that Michael has an older sister (age 18) and a brother (age 20), both in good health. Michael's father died at age 39 in a car accident after a sudden heart attack at the wheel and Michael's paternal first cousin died while playing tennis at the age of 15.

Case # 1 Pedigree



Case #1 Outcome Cont.:

- This family history is suggestive of an autosomal dominant type of cardiomyopathy for which Michael's siblings and other family members are at risk. This information helps provide family members with a more accurate risk assessment, and allows for medical intervention and careful monitoring of affected and at-risk relatives, such as Michael's two siblings.

Lifetime & increased risks for selected adult cancers

- **Breast cancer: General population lifetime risk: 12.3%**

  Women are considered at increased risk if they have:
  - A mother, sister(s), daughter(s) with breast ca, especially if dx. < 50
  - A father &/or paternal relatives (grandmother or aunts) with breast ca, especially if dx. <50
  - Maternal relative (grandmother or aunts) with breast cancer, especially if dx. <50
  - A family history of breast &/or ovarian ca &/or colon and rectum ca in multiple generations

- **Ovarian cancer: General population lifetime risk: 1.4%**

  Women are considered at increased risk if they have:
  - A mother &/or sister(s), daughter(s) or grandparent(s) with breast &/or ovarian ca, especially if one or more is dx. < 50
  - A personal or family history of breast, endometrial, or colorectal cancer

Eberl, MM, et al. Journal of Am Board of Family Practice 2005; 18:211-217
SEER Cancer Statistics Review, 1975-2004, National Cancer Institute

Lifetime & increased risks for selected adult cancers

- **Colon cancer: General population lifetime risk: 5.4%**
  Individuals are considered at increased risk if they have:
  - A 1st degree relative with ca of the colon or rectum
  - A maternal or paternal relative with colorectal ca, especially if dx <50
  - A family history of multiple generations affected by ca of the uterus, breast, &/or ovary among 1st or 2nd degree relatives

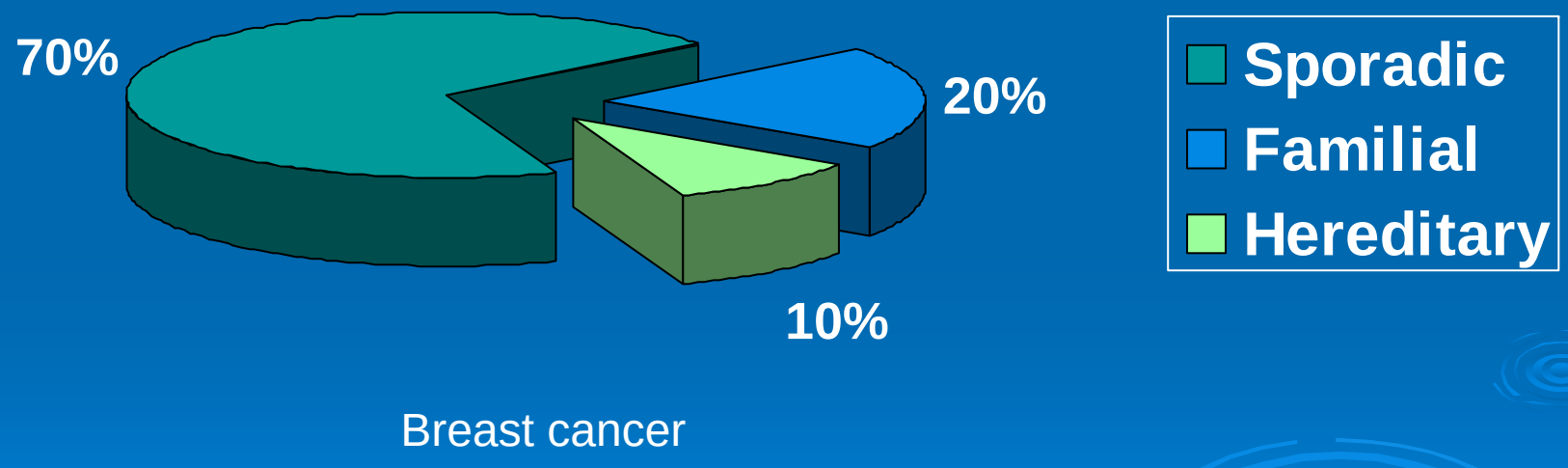
- **Prostate Cancer: General population lifetime risk: 16.7%**
  Men are considered at increased risk if they have:
  - A father, brother, or son with prostate ca
  - A mother or sister with ovarian ca
  - A family history of breast &/or ovarian ca(s) among 1st or 2nd degree relatives

Eberl, MM, et al. Journal of Am Board of Family Practice 2005; 18:211-217
SEER Cancer Statistics Review, 1975-2004, National Cancer Institute

Hereditary Cancer Risk Assessment and Genetic Counseling

- Full pedigree analysis and risk assessment
- Discussion of:
  - Personal cancer risks based on family history
  - Genetic testing options and risk of mutation
  - Benefits, risks and limitations of genetic testing
  - Personalized, risk-based screening and screening options
  - Support resources

How much breast cancer is hereditary?



Breast cancer

Myth:

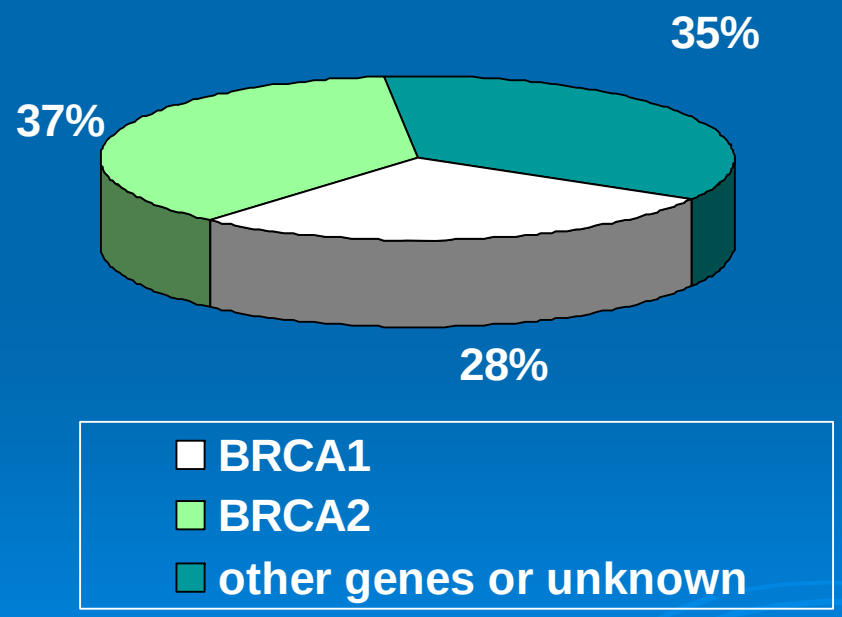
- A person with cancer must have the gene mutation.

Fact:

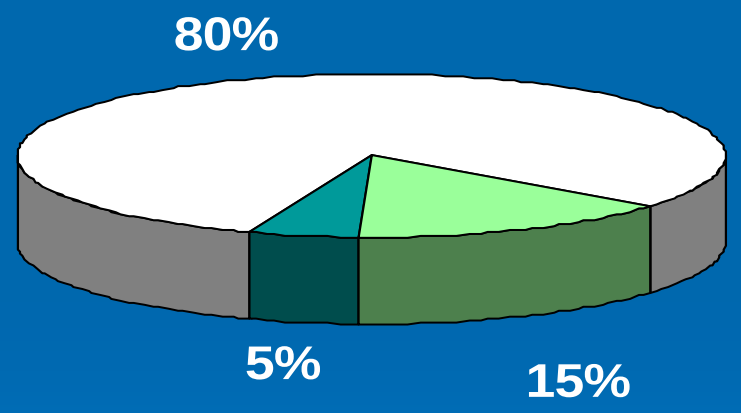
- Hereditary breast and ovarian cancer is rare.

Causes of inherited susceptibility to breast cancer

Families with site- specific breast cancer



Families with breast and ovarian cancer

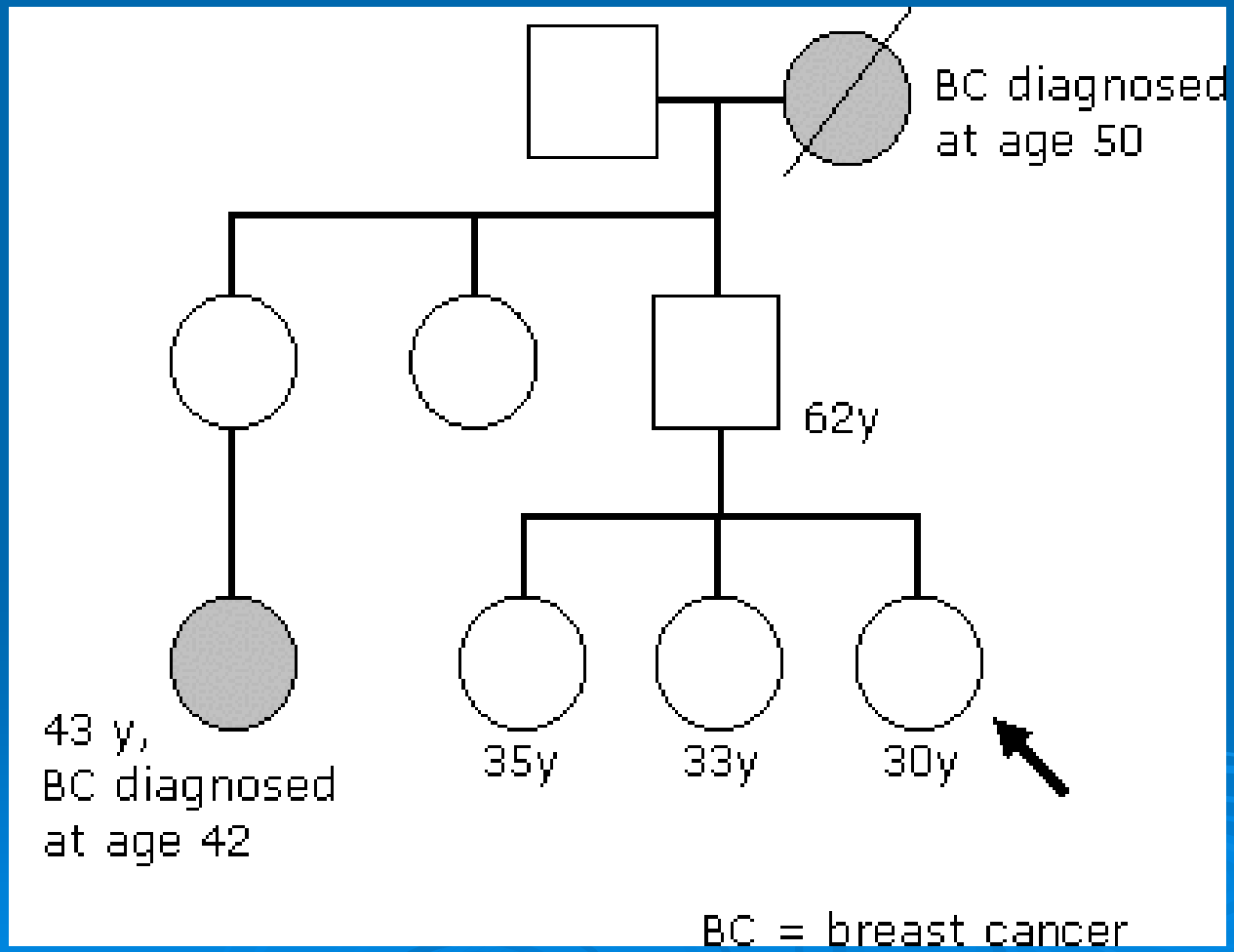


Ford D. et al. Am J Hum Genet. 1998;62:676-689

Case #3:

- A 30-year-old Jewish woman asks about the "breast cancer gene." She read that Jewish women may be more likely to have this “gene”. Her paternal grandmother & aunt’s daughter both had breast cancer at 50 and 42, respectively. She assumes their cancers do not affect her risk. Her father is in good health at 62.

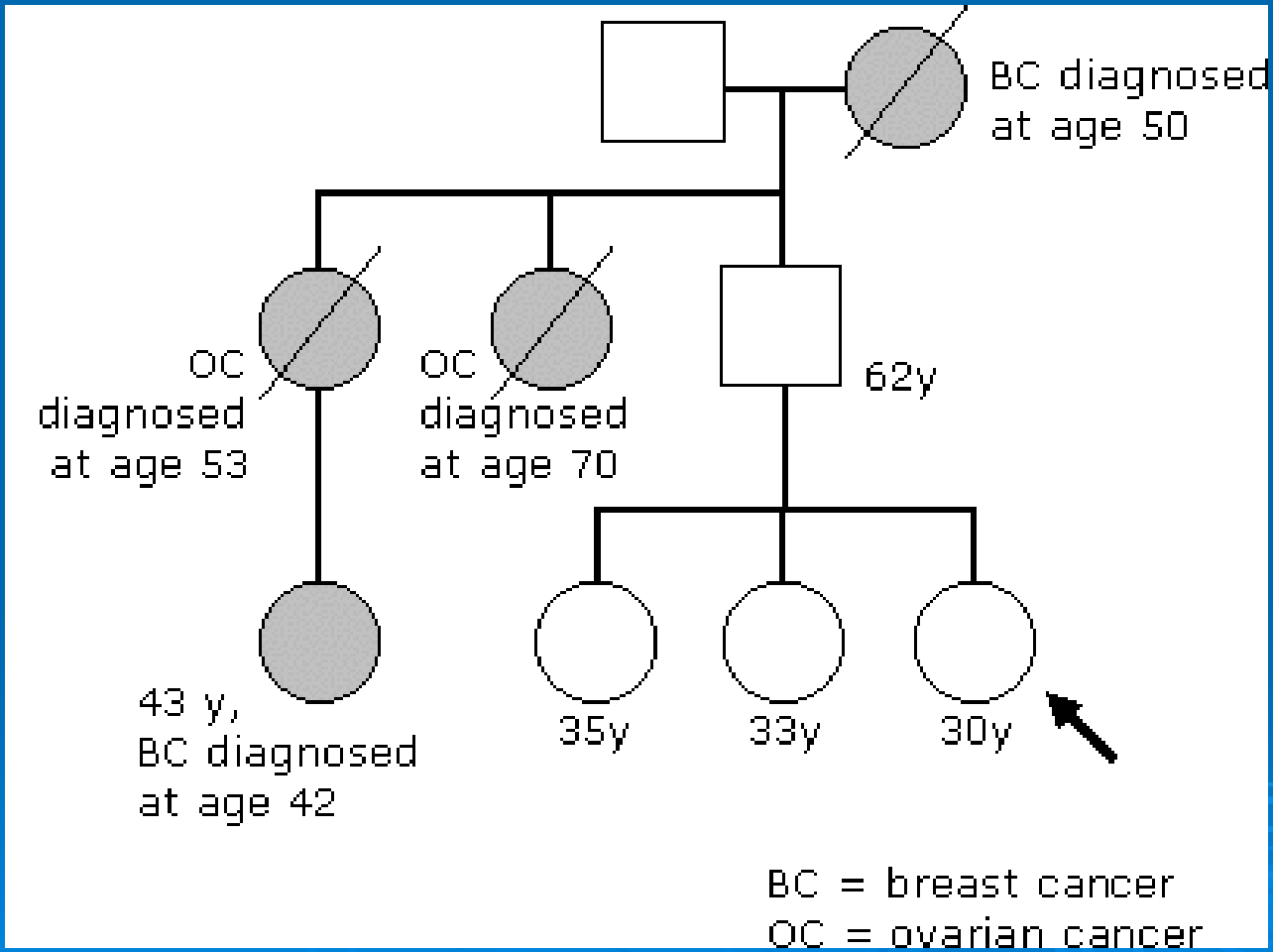
Case #3 pedigree:



Case #3 points to consider:

Q. What if further exploration of family history reveals additional cases of cancer? Let's assume that further exploration of the family history reveals ovarian cancer in two relatives, as follows:

Case #3 new pedigree:



Case #3 Outcome Cont.:

A. This additional family history is significant, because it greatly increases the likelihood that a *BRCA1* or *BRCA2* mutation is present in the family.

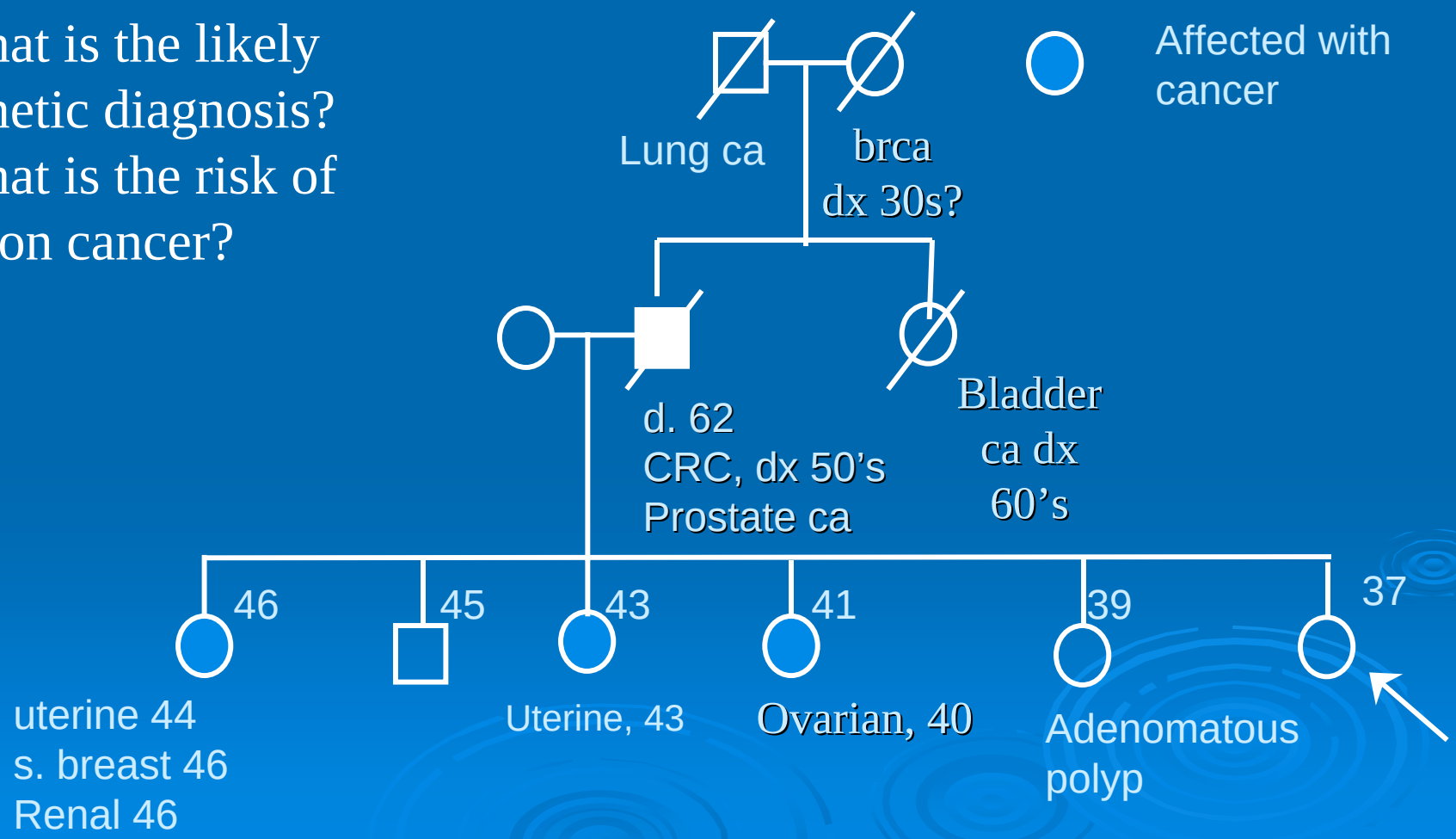
- Refer to a genetic counselor for possible genetic testing.

www.genetests.org

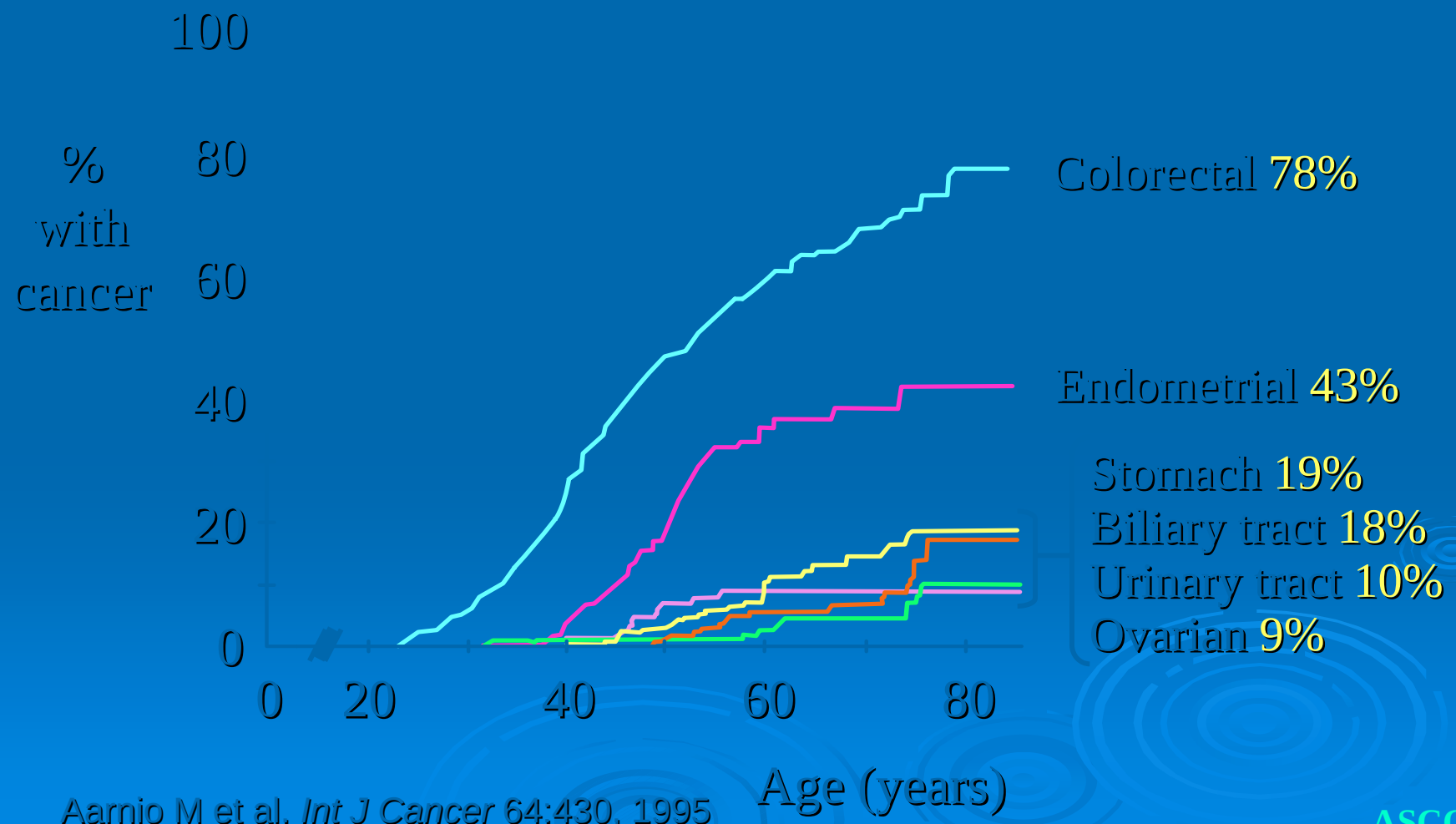
Characteristics of Hereditary Colorectal Cance

- Multiple relatives with colorectal cancer
  - One or more diagnosed at an early age (<50)
- Sequential generations affected
- Other cancers in the family known to be associated with CRC (uterine, ovarian, GI)
- Multiple primary tumors or multiple adenomatous polyps
- EGAPP recommendations to study tumor

Would you refer this patient?
What is the likely genetic diagnosis?
What is the risk of colon cancer?



Cancer Risks in HNPCC



Aarnio M et al. *Int J Cancer* 64:430, 1995

ASCO

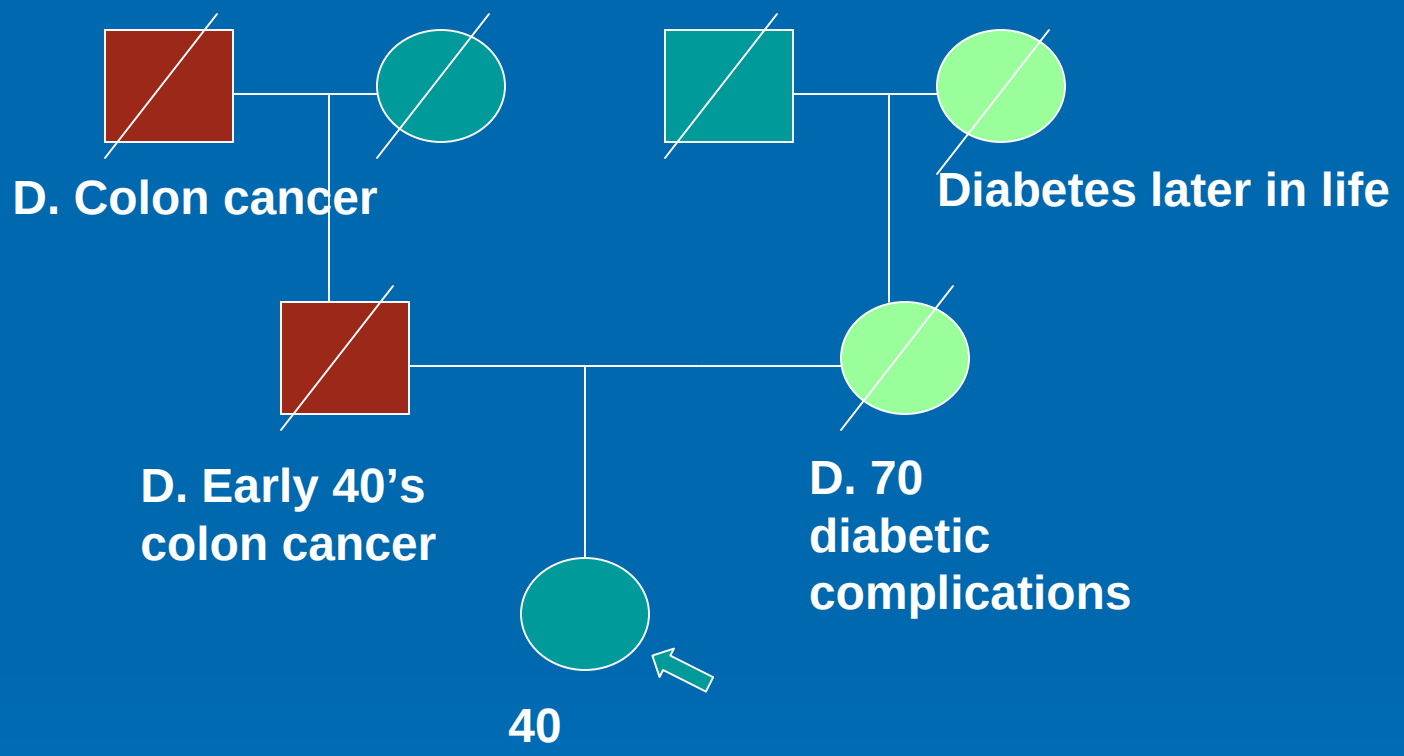
Case #4:

A healthy 40 year old woman requests diabetes testing, as “it runs in her family.”

Her mother died at age 70 of diabetic complications and her grandmother developed diabetes late in life. The patient also mentions that her father died in his early 40s of colon cancer, and her paternal grandfather had colon cancer.

Q: How does family history help you to treat this patient?

Case #4 Pedigree



Colon cancer

Diabetes

Case #4 Outcome:

A: Based on this information, you recommend screening for diabetes AND colon cancer. The patient is shocked, assuming colon cancer "only runs in the men in our family."

Family history allowed an opportunity to screen this patient for all conditions for which she is at risk, and provided an opportunity for education about the genetics of colon cancer.

Case #5:

- A 45 yr. old male patient, Mr. Y has come to discuss an upsetting incident while on vacation. While away, he found himself unable to remember the name of his hotel while out jogging. He had to call home and ask his daughter for help.

Case #5 Cont.:

- He denies drug use of any kind, drinks moderately, and recently had an annual physical examination, with all results normal. He jogs 30 minutes a day. Physical examination is unremarkable. There are no focal neurological signs. He is unable to remember three objects. He knows his name and telephone number but has trouble with his birthday, his address, and the name of the President of the U.S.

Case #5 Cont.:

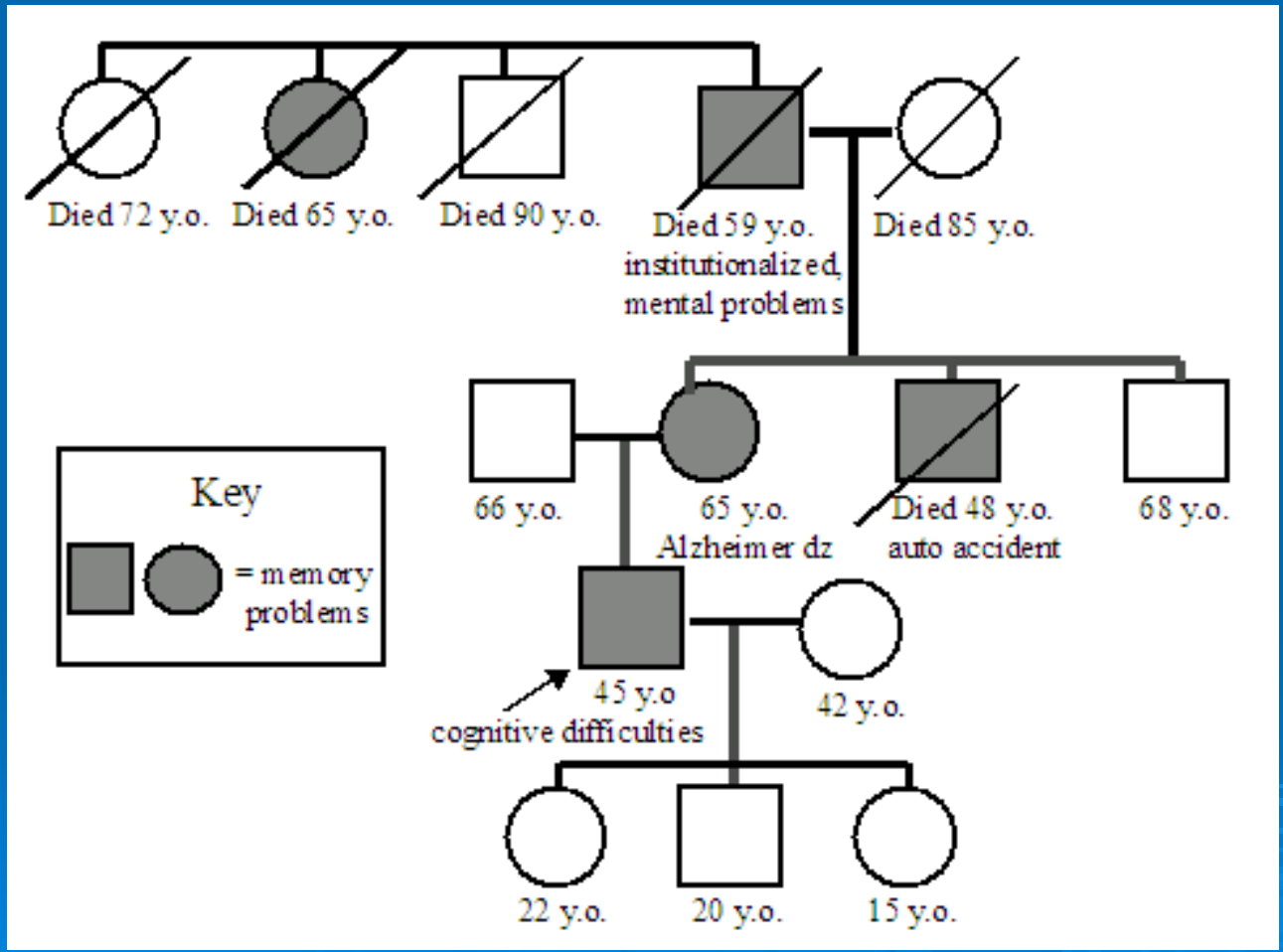
Asked to describe the details of what happened in San Francisco, he says, "The same thing happened to my mother." He has difficulty telling his mother's story. Mrs. Y explains that Mr. Y's mother, age 65 years, has been in a nursing home for the past five years, with a diagnosis of Alzheimer's disease. She also notes that Mr. Y has been under considerable pressure at work, with his boss finding his performance unsatisfactory.

Q. How can family history help treat this patient?

Case #5 Outcome:

A. A three-generation family history would be helpful in determining the likelihood of autosomal dominant early-onset AD in Mr. Y's family.

Case #5 Pedigree:



Case #5 Outcome Cont.:

- This family history is consistent with autosomal dominant inheritance of early-onset Alzheimer's disease.
  - Disease occurs in successive generations
  - Both males and females are affected. In each generation, approximately equal numbers of individuals are affected and unaffected
  - Given his symptoms and his family history, Mr. Y has early-onset autosomal dominant Alzheimer's disease and should be referred for genetic counseling

Asthma

- In a large survey of 33 studies, a family history of asthma in one or more first-degree relatives was consistently identified as a risk factor for asthma
- Asthma is more prevalent in Hispanics and African-Americans than Caucasians in USA
- Asthma is more prevalent in boys than girls

Burke, Wylie et al, Am J Prev Med, Vol. 24, (2), Feb. 2003, Pgs 160-169

Type 1 Diabetes

- Background population risk: 1/50-1/100
- Average risk to sibs: 1/17
- Offspring of a male with Type I diabetes have 1/17 risk
- Offspring of a woman diagnosed <25 years old is 1/25; but offspring of woman >25 years is 1/100
- Risk for child doubles if parent developed diabetes before 11 years of age
- If both parents have diabetes, child's risk is 1/4 to 1/10

www.diabetes.org/genetics.jsp

Type 2 Diabetes

- 5.7% prevalence
- Higher in Hispanics, Native Americans, African-Americans, and Pacific Islanders
- Risk for child is 1 in 7 if parent was diagnosed before age 50 and 1 in 13 if parent was diagnosed after age 50

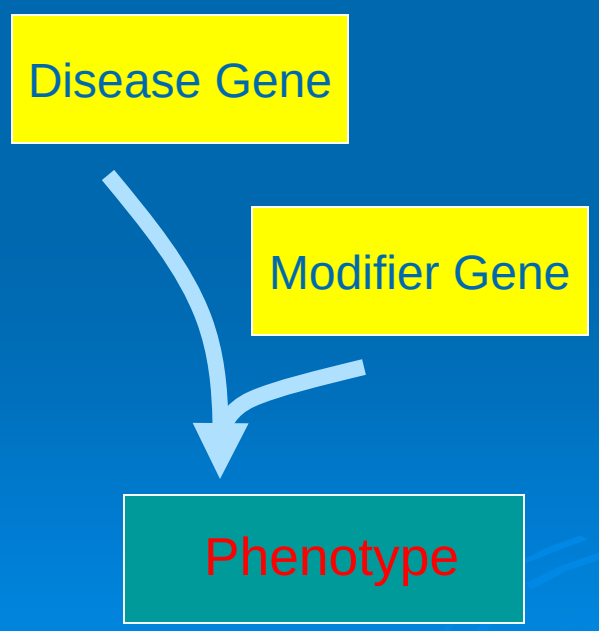
www.diabetes.org/genetics.jsp

Why Is This Important Now?

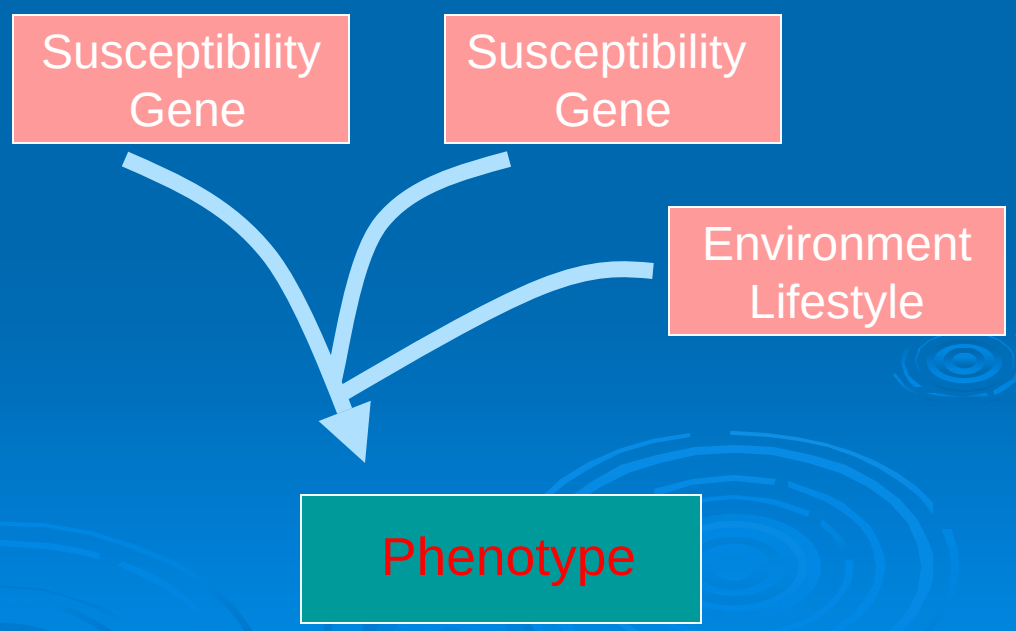
- Personalized medicine is coming
- Direct-to-consumer marketing of genetic tests
- Pharmacogenetics/ Pharmacogenomics
- Medicolegal Issues
- Limited availability of genetic professionals
- Empowers patients

Inheritance Models

Monogenic, Mendelian (simplex)



Complex, multifactorial, multigenic



Barriers to Use of Family History

- Lack of time
- Underestimation of its utility
- Lack of reimbursement/high cost of services
- Need for a good tool to facilitate process
- Lack of genetic knowledge
- Unsure what to do with information
- Skepticism about the impact of genetic discoveries
- Skepticism about validity/utility of genetic testing
- Ethical, legal and social concerns

To Review -Family History Important Components

- At least three generations
- Maternal and paternal sides
- Current age/ age at death
- Cause of death
- Relevant medical conditions
- Cardiovascular disease
- Obesity
- Hypertension
- Site and age at onset for primary cancer

Family History: Important Components Cont.

- Age of onset of diseases
- Birth defects
- Hearing loss
- Mental retardation
- Miscarriages/
- stillbirths
- EtOH/ tobacco
- Ethnicity of all 4 grandparents
- Consanguinity
- Note negative/ unremarkable family history
- Record date taken and by whom
- Update regularly

Red Flags

- Several closely related individuals affected with the same or related conditions (e.g. breast and ovarian cancers)
- Sudden death in someone who seemed healthy
- Individual or couple with 3 or more pregnancy losses
- Medical problems in children of parents who are closely related (second cousins or closer)

More Red Flags

- A common disorder with earlier age of onset than typical, especially if it occurs in multiple family members.
  - Ex: Breast cancer: < age 45-50 years (premenopausal)
  - Colon cancer: < age 45-50 years
  - Prostate cancer: < age 45-60 years
  - Vision loss: < age 55 years
  - Hearing loss: < age 50-60 years
  - Dementia: < age 60 years
  - Heart disease: < age 40-60 years
  - Stroke: < age 60 years

What You Need to Know Cont.

- Appreciate implications that information on genetic background can have on a person's self-image, family relationships and social status and that reactions may differ depending on gender, age, culture and education
- Be aware of need for appropriate referrals to genetic and community support groups
- Recognize your limitations and seek consultation when necessary
- Commit to a program of lifelong learning

Adapted from AMA pamphlet:
Family medical history in disease prevention. 2004.

What Do I Do with the Information?

- Review family history with patient
- Consult with a genetic professional
- Refer to a genetic professional
- Ongoing communication with patient and specialists as needed
- Update family history regularly

You Can Make a Difference!

- An observational study of primary care physicians indicated that family histories were discussed about 50% of the time at new visits and 22% of the time during follow-up visits.
- However, the average duration of family history discussions was less than 2.5 minutes.

Acheson LS, et al Genet Med 2000;2:180-5.

Efficacy of Family History

- Using family history to identify people at moderate or high risk for common chronic diseases may augment current efforts to motivate patients to adopt healthier lifestyles and participate in screening and prevention programs.

Yoon, P.W., et al, Am.J Prev Med 2003;24(2)

Take Home Message

"Think genetically, act accordingly"

AAFP, 2005

Acknowledgements

- **Holly Nee, MS, CGC, Lisa Tuttle, MS, CGC, Irene Rainville, MS, CGC and Meagan Krasner, MS, CGC** for research, development and review of slides
- **NERGG, Inc**. for technical support
- **HRSA** Supported in part by a grant from the Genetic Services Branch of the Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA) and the NEW ENGLAND REGIONAL GENETICS AND NEWBORN SCREENING COLLABORATIVE, HRSA GRANT #1U22MC03959
- **NSGC** slide show
- **NEPHGEC** members for their guidance and input
- CDC website for images and ideas

How to Locate a Genetic Professional in Your Area:

- Many major hospitals and medical centers have board certified medical geneticists, certified GCs or advanced practical nurses in genetics on staff
- Fully searchable international directory at www.geneclinics.org
- American Board of Medical Genetics (www.abmg.org)
- American College of Medical Genetics (www.acmg.net)
- National Society of Genetic Counselors (www.nsgc.org/resourcelink.asp)