Genetics and Genomics: Relevance to Clinical Practice

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Overview of the Session

- Human Genome Project
- Relevance to Clinical Practice
  - Genomics and Personalized Healthcare
  - Pharmacogenomics
- Differences between Genetics and Genomics
- Activities
- Clinical Implications
- Questions
Objectives

- Articulate the differences between genetics and genomics and epigenetics
- Discuss how this burgeoning area of science influences nursing
- Discuss ethical, legal, and social issues related to genetics and genomics
- Identify at least one issue of relevance in the field of genetics and genomics that concerns you in your practice area
Lifelong Learning
Genetics and the Public
News regarding genetics
UC Berkeley DNA swab

New York Times
May 21, 2010

- Incoming Freshman Class of 2014
- Voluntary DNA sample
- Test for 3 genes that help regulate the ability to metabolize alcohol, lactose and folates

- Concerns
  - Issues of confidentiality
  - Mass testing without counseling support
  - Interpretation of Results
    - If no marker for alcohol metabolism would encourage the potential to drink more
Internet: Genetics and Health

7,020,000 Sources  May 22, 2010

92,300,000 Sources  on September 22, 2011

98,600,000 Sources  on November 3, 2014
Genetics and Genomics.....

Our Responsibility to Continuing the Journey in Lifelong Learning

Genetics

THE FUTURE IS NOW

New breakthroughs can cure diseases and save lives, but how much should nature be engineered?
More importantly is the subject of Genomics as opposed to Genetics....

What, you might ask is the difference between Genetics and Genomics?
Genetic Health Care

- Is based on understanding the impact of single genes on disease...
Clinical Examples of Genetic Health Concern

- Down’s Syndrome
- Sickle Cell Anemia
- Fragile X Disease
Genomic Health Care

- Is based on understanding the impact of our entire genome and environmental factors on disease and health...
Genomic Health Care

1. Heart Disease (654,000 deaths in 2004)
2. Cancer (550,000)
3. Cerebrovascular diseases (150,000)
4. Chronic lower respiratory disease (124,000)
5. Injury? (109,000)
6. Diabetes (73,000)
7. Alzheimers disease (66,000)
8. Pnuemonia/influenza (43,000)
9. Kidney disease (43,000)
10. Septicemia (33,000)

(ICU implications)
Genomic Health Care

1. Heart Disease
   1. Prolonged QT
   2. Cardiomyopathy
      1. Hypertrophic
         1. 11 genetic mutations with increased risk SCD
      2. Dilated
         1. 14 genetic mutations
      3. Restrictive
   2. Cerebrovascular diseases
      1. Warfarin Metabolism (CYP450)
      2. FDA requiring testing CYP450 to release
      3. Septicemia (33,000)
Genomic Health Care

- Is built on the foundation of the Human Genome Project...
Human Genome Project

- **identify** all the approximately 20,000-25,000 genes in human DNA
- **determine** the sequences of the 3 billion chemical base pairs that make up human DNA
- **store** this information in databases
- **improve** tools for data analysis
- **transfer** related technologies to the private sector
- **address** the ethical, legal, and social issues (ELSI) that may arise from the project
Human Genome Project

- An international government project that ended ahead of schedule!!!!
- And under budget!!!
- And from its start earmarked funds for consideration of its ethical, legal and social implications (ELSI)....the largest amount of funding ever devoted to bioethics
Genomic Health Care

- Will change health care by….
  - Creating a fundamental understanding of the biology of many diseases, even many “non-genetic” ones
  - Leading to defining disorders by biology of causation, rather than symptoms

Symptoms → Treatment
Prevention ← Causation
Genomic Health Care

Knowledge of individual genetic predispositions will allow:

- Individualized screening
- Individualized behavior changes
- Individualized presymptomatic medical therapies, e.g., antihypertensives agents before hypertension develops, anti-schizophrenia agents before schizophrenia develops
Genomic Health Care

- Will change health care by
  - Creating pharmacogenomics, including:
    - The right drug, at the right dosage, for the right patient
  - New drug targets
A Fun Fact: How Many Human Genes Do ALL Current Drugs Target?

1. ~500 (2.5% of the genome)
2. ~1000 (5%)
3. ~5000 (25%)
4. ~10,000 (50%)
5. ~15,000 (75%)
6. ~20,000 (100%)
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Cumulative Pace of Disease Gene Discovery 1981-2005

Source: Online Mendelian Inheritance in Man
An early result from the HapMap: Age-Related Macular Degeneration…

three genes appear to account for approximately 74% of the attributable risk of AMD in older adults……

and we did not even view this as a particularly “genetic” disorder……
Gene Discoveries for Common Complex Diseases

NIH Research Initiatives

- Human Genome Project Begins
- Human Genome Project Completed
- HapMap Project Initiated
- HapMap Project Completed
- Macular Degeneration
- The Cancer Genome Atlas Launched
- Genetic Association Information Network Launched
- Genes and Environment Initiative Launched
- Type 2 Diabetes
- Prostate Cancer
- Systemic Lupus Erythematosus
- Myocardial Infarction
- Inflammatory Bowel Disease
- Macular Degeneration
- Psoriasis

YR 90 91 92 93 94 95 96 97 98 99 00 01 02 03 04 05 06 07
What Else is Going on in Genomics?

- A small sampling......
  - Personalized Medicine
  - Pharmacogenomics
  - Health Policy Issues
    - GINA (Genetic Information Nondiscriminatory Act, 2008)
Goal of Personalized Medicine

- Help us achieve the right diagnosis and prescribe the right medication for the particular individual and exact condition, steadily improving on traditional trial-and-error approaches;

- Enable us to spot the onset of disease even before symptoms appear, and take action to preempt or delay onset of the condition; and

- Help us identify our own predisposition to disease, so that we can take more effective steps to prevent it.
Prologue by HHS Secretary Michael O. Leavitt

Some Key Points:

- Developed powerful pharmaceuticals – yet most drugs prescribed in the US today are effective in fewer than 60% of treated patients. This efficacy rate reflects the variability of metabolism or other factors from person to person.

- Our definitions of diseases remain rooted in 18th and 19th century terms.
Every year, over 106,000 people in the United States die from adverse reactions to correctly prescribed doses of drugs.

Another 2.2 million suffer serious, but not deadly, side effects.
Emergency Department Visits

- Centers for Disease Control National ED Surveillance 2004-2005
- Adverse drug events (ADE) defined as undesirable pharmacologic or idiosyncratic effects from medications administered at **correct** dosages.
  - ADE’s accounted for > 200,000 ED visits
  - ADE’s accounted for > 36,000 hospitalizations
  - Among individuals ≥65 y/o 17.3% of ED visits were associated with ADE’s from **warfarin**.

Research for the future: Personalized medicine

Goals for personalized medicine:

- Identify genetic differences between people that affect drug response
- Develop genetic tests that predict an individual’s response to a drug
- Tailor medical treatments to the individual
  - Increase effectiveness
  - Minimize adverse side effects

Pharmacogenetics
Evaluates how an individual’s genetic makeup corresponds to their response to a particular medication.

Pharmacogenomics
Combines pharmacogenetics with genomic studies. Uses large groups of patients to evaluate how candidate drugs interact with a range of genes and their protein products.
Personalized Medicine

- Drug toxic but beneficial
- Drug toxic but not beneficial
- Drug not toxic and not beneficial
- Drug not toxic and beneficial

Patient group

Same diagnosis, same prescription
Drug Response based on Genotype

- **Genotype A**
  - No Response to Drug X

- **Genotype B**
  - Side Effects outweigh the benefits

- **Genotype C**
  - Optimal Response
DRUGS OF THE FUTURE
Amazing new medicines will be based on DNA
Find out how they will change your life
What about Personalized Medicine and Specific Product Availability:
Direct to Consumer Marketing

Two Separate Issues

- Claims made about the tests to induce purchase (e.g., through advertising);

- Sale of genetic testing services and provision of test results directly to consumers

http://www.navigenics.com/
http://www.decode.com/
Direct to Consumer Marketing

23andMe

- 23andMe launched directly to consumers in December 2007.
- Saliva Sample.
- Evaluating nearly 600,000 SNP’s (Single Nucleotide Polymorphism) for 90 health conditions $399.

http://www.23andme.com
Time’s Best Inventions of 2008

October 30, 2008 – TIME Magazine announced that the Personal Genome Service™ from 23andMe, Inc. has been named 2008's Invention of the Year.

http://www.time.com/time/specials/packages/article/0,28804,1852747_1854493,00.html
How Prevalent is the Uptake?

The New York Times

Fashion & Style

When in Doubt, Spit It Out

A DATE WITH DHA
K. C. Dustin and his wife, Debra Netschert, give saliva samples.

By ALLEN SALKIN
Published: September 12, 2008
Pathway Genetics is Expected to Sell Genetic Testing Kits through Walgreens Stores

New York Times
May 11, 2010

“Genetic tests that assess a person’s risk of getting various diseases are heading to the corner drug store.”

- **Product:** “Discover your DNA”
- **Cost:** $20-$30 (plus $79-$249 test)
- **Commerce:** consumer info vs medical test
  (State laws will govern this)

Walgreens postpones carrying genetic test kit

LA Times May 13, 2010
Personal Genome Project

http://www.youtube.com/watch?v=mVZI7NBgcWM (7:21)
Availability of Genetic and Genomic Testing

- Prenatal diagnosis
- Carrier testing
- Confirmation of a genetic diagnosis
- Genetic susceptibility
- Disease screening/diagnosis
- Pharmacogenomics
- Disease profiling
Genetics and Genomics

Genetic Engineering, Genetic Report Cards, Pharmacogenetics may all contribute to improving our health………...but what about the ethical considerations associated with this information

For example: Your son or daughter is a scholar athlete but their genome indicates that they are at risk for sudden cardiac death (SCD) so they never get the Division 1 offer to play basketball........

Is this ethical???????
GINA (Genetic Information Nondiscrimination Act)

- Signed into Law 5/08
- Effective Date 11/09

Do what does this mean for us as health professionals....

- **Responsibility to our patients/clients:**
  - Clinical Care
  - Knowledge
  - Referral

- **Responsibility to ourselves:**
  - Continued Knowledge Attainment

- **Responsibility to our profession:**
  - Engagement
  - Advocacy
The Essential Nursing Competencies and Curricula Guidelines for Genetics and Genomics

- Define essential genetic and genomic competencies for ALL nurses regardless of level of academic preparation, practice setting or specialty.
  - Guide curriculum content based on the current state of the evidence.
  - Provide the basis for evaluating nurse competence in genetics and genomics including:
    - NCLEX
    - Certification
    - Maintaining Licensure

- Prepare the nursing workforce to deliver competent nursing care in the genomic era of healthcare.
Role as Critical Care Nurses

Critical Care Nurse
The journal for high acuity, progressive, and critical care nursing

Essential Nursing Competencies for Genetics and Genomics: Implications for Critical Care
Lynnette Howington, Kristina Riddlesperger and Dennis J. Cheek

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Published online http://www.cconline.org
Genetics and Genomics for Health Professionals – New NHGRI Web Resource

- Curricular resources
- New NIH and NHGRI research activities
- Related ethical, legal and social issues
  - http://www.genome.gov/Health/
- Reliable, up-to-date genetics and genomics information related to patient management
NIH and Human Genome Research Institute
Genetic and Genomic Competency Center

http://www.g-2-c-2.org/
The Angelina Jolie Effect

DOUBLE MASTECTOMY
Let’s look at some specific genetic discoveries

- [http://www.dnai.org/d/index.html](http://www.dnai.org/d/index.html)

And a tool to address Family History:

- [https://familyhistory.hhs.gov/fhh-web/home.action](https://familyhistory.hhs.gov/fhh-web/home.action)
What about genomic health and the epigenome

- [http://www.youtube.com/watch?v=Xjq5eEs1Jhw](http://www.youtube.com/watch?v=Xjq5eEs1Jhw) (7 minutes)

- [http://www.youtube.com/watch?v=wFsxVkuChdU&feature=related](http://www.youtube.com/watch?v=wFsxVkuChdU&feature=related) (6 minutes)
Genetic Manipulation

- The Genome ...... the hardware
  - Inherited

- The Epigome ...... the software
  - Can alter
Implications

- As an RN?
- As a Critical Care Nurse?
- As an Advanced Practice Nurse or Administrator?
- As a researcher?
- As a healthcare consumer?
Betty’s Story in 2019

◆ Betty completes the Surgeon General’s family history tool at age 18, learns of three uncles with early heart disease

◆ She consults her health care team, who suggest complete genome sequencing for $1000

◆ She inquires about the risk of genetic discrimination, but federal legislation has outlawed this
Betty’s Story Continues

- She is found to have five gene variants that well validated studies have conclusively shown increase risk of early heart-attack three fold

- She and her health care team design a program of prevention based on diet, exercise, and medication precisely targeted to her genetic makeup
Betty’s Story Continues

- Betty does well until age 75
- She develops left arm pain that she assumes is due to gardening, but her primary care provider knows her higher risk and diagnoses an acute MI
- Referring to her genome sequence, the drugs that will work best to treat her are chosen
- She survives and is alive and well in the 22nd century
Personalized Health Care: Could the Dream Become a Nightmare?
Betty’s Story Gone Wrong

- The Surgeon General’s Family History Initiative never really takes off and her primary care team are too busy filling out insurance forms to ask about family history, so Betty never learns about family history.
- Betty is offered genome sequencing but after seeing her brother lose his long-term care insurance from this information, she declines.
Betty’s Story Gone Wrong

- Betty eats an unhealthy diet, gains weight, and develops hypertension.
- While tests to predict which drug would be most effective for Betty have been proposed, they have never been validated, and are not reimbursed.
- Betty’s hypertension is treated with a drug that causes a hypersensitivity reaction, so she stops treatment.
Betty’s Story Gone Wrong

◆ After 10 years of uncontrolled hypertension, Betty develops left are pain at age 45
◆ Her primary care team, unaware of her high risk, assume this is musculoskeletal and prescribes rest
◆ Betty returns to the ER the next day in cardiogenic shock
Betty’s Story Gone Wrong

- The absence of her genome sequence information prevents optimal choice of therapy
- Betty dies in the ER at age 45
Revisiting Our Objectives

- Articulate the differences between genetics and genomics and epigenetics
- Discuss how this burgeoning area of science influences nursing
- Discuss ethical, legal, and social issues related to genetics and genomics
- Identify at least one issue of relevance in the field of genetics and genomics that concerns you in your practice area
Clinical Implications

◆ Sepsis

◆ Genetic makeup has been identified as a main factor leading to the development of sepsis, an inflammatory reaction that affects the whole body (systemic) that occurs during infection. When associated with organ dysfunction, sepsis is considered severe.

◆ In June issue of Anesthesiology scientists take aim at identifying genetic risk factors for sepsis
What is this?
Current Crisis: Ebola

Individual genetic differences may affect Ebola survival. (AP Photo/Baba Ahmed)
The Ebola Virus

The Ebola Virus on a cell

Genetic Relevance

- Relationship between genes and the virus
- Genetic diversity and range of Ebola Symptoms
- Study in Mice bred with high genetic diversity:
  - Resistant
  - Some Symptoms but survived
  - Similar to Typical Lab Mice: No symptoms but died

Credit: CDC/ NIAID
What does this mean for humans?

Plasma transfusions presumably transferring antibodies
“Genomics offers the opportunity to better understand the role of genes, environment and behavior as risk factors for complex chronic disease”

State of Michigan Genetics Plan
Uh, yes... I was able to trace your ancestry... but remember... I'm only the messenger here...
Thank You!
If you look deeply into the palm of your hand, you will see your parents and all generations of your ancestors. All of them are alive in this moment. Each is present in your body. You are the continuation of each of these people.

-Thich Nhat Hanh