Race and Genetics:
How different cultures mediate issues of testing, prevention, and treatment

(Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations)

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Sickle Cell Disease, Tay-Sachs Disease, and Cystic Fibrosis

What do the histories of these three diseases tell us about race/ethnicity and genetics?

About vulnerable populations?

About the genetic detection, prevention, testing, and treatment (from era of genetic testing... to era of gene therapy and gene editing)?
TSD, SCD, and CF – common features

Autosomal Recessive (established in 1950s)

Mechanisms of Inheritance (carriers → disorder)

Prevention via Genetic Testing/Counseling (1970s)

Identification of cause/Hope for Treatment: - Drugs, Surgery: Impact on Life Expectancy, Illness, Experience (1950-present)

THREE CAUTIONARY TALES
Genetic Progress and Social Complexities

Each genetic disease – travels different pathways because of questions of race and ethnicity
1910 – Sickle Cell clinical description (by James Herrick)

1950 – Linus Pauling discovery that a missubstituted amino acid on the complex hemoglobin molecule caused sickling (turned the disease from an obscure curiosity into the “first molecular disease”)

SEARCH FOR A “DE-SICKLING” AGENT:

One scientist predicts in 1951, medicine “may be able to devise a small innocuous molecule which might lock on to the defective hemoglobin and prevent the abnormal molecule from misbehaving.”

UREA – 1970s promising desickling agent shows “no hematological of clinical benefit,” toxic side effects. 1990s: Hydroxyurea success (reduce painful crises
TESTING – PROGRESS OR STIGMA?

LINUS PAULING, UCLA Law Review, 1968: “I have suggested that there should be tattooed on the forehead of every young person a symbol showing possession of the sickle cell gene or whatever other similar gene… that he has been found to possess in a single dose… If this were done, two young people carrying the same seriously defective gene in single dose would recognize the situation at first sight, and would refrain from falling in love with one another.”

Rising awareness of SCD: “disease of pain and suffering” of African-Americans, too long ignored

Carrier frequency: 1 in 12 African-Americans
Sickle Cell Disease Therapeutic Progress

- Antibiotics
- Transfusion
- Prophylactic Penicillin
- Hydroxyurea (treatment of crises)
CARRIER TESTING AND DISCRIMINATION – IMPLICATIONS FOR EMPLOYMENT

• AIR FORCE ban on TRAIT CARRIERS; Airlines and carriers as flight attendants (1970s)

THE HEALTH OF SCD CARRIERS (at WORK, at ALTITUDE, under STRESS)?

Screening U.S. College Athletes for their Sickle Cell Disease Carrier Status, October 11, 2010 (Secretary’s Advisory Committee on Heritable Disorders in Newborn and Children) ---- to advise the Secretary of the U.S. Department of Health and Human Services about the rule of the National Collegiate Athletic Association requiring testing for sickle cell trait in all incoming Division I student athletes.

ONGOING ETHICAL AND POLICY CONTROVERSY:

Is a ban/restriction on carriers a form of discrimination against or social policy in their best health interest?
Tay-Sach’s Disease: A Success Story (Warren Tay and Bernard Sachs) 1880s

“The Genetic Basis of Jewish Amaurotic Family Idiocy”

“almost exclusively observed among Hebrews”

neurological and cognitive decline, mental retardation, cerebral seizures, loss of vision and motor control, death by age 2-6.

AT MID-20th CENTURY

1950s: Rise of clinical genetics, discovery and identification of the heterozygote (carrier) possible; identified as lipid storage disorder, lysosomal storage disease

Carrier frequency: 1 in 25/30 Ashkenazi Jews

1969: O’Brien and Okada – deficiency of hexosaminidase A (hex A) which results in buildup of lysosomes in brain tissue.

Hope for a cure: 1971 -- “with detection and prevention of TSD possible, the question of cure arises…” Friedman
Cure: By 1982 – “Protein Targeting” in TSD

DEEMED A FAILURE

O’BRIEN: “The prospects for the development of therapy in the near future are dismal”

The Question of Prevention: INTERTWINED WITH JEWISH IDENTITY in U.S.

Despite Carrier Frequency (TSD)
1 in 25-30 Ashkenazi Jews
1 in 20 French Canadians/Louisiana Cajuns
1 in 200-300 U.S. population
One notable episode: RACE, ETHNICITY, AND GENETICS

TESTING SERVING THE NEEDS of ethnic/religious community

1983 -- RABBI JOSEF EKSTEIN (had watched four of his own Tay-Sachs children die)

FOR ULTRA-ORTHODOX JEWISH, proscription against abortion limits options

Rabbi Ekstein’s Innovation: CHEVRAH DOR YESHORIM “GENERATION OF THE RIGHTEOUS”

Testing Adolescents for Carrier Status – Arranged Marriages to avoid producing TSD

SUCCESS SPREADS: Chicago – “modern matchmaking..helps avert genetic disease”
FROM DREAM TO NIGHTMARE – PREVENTING CF?

“this mentality, unfortunately, has been fostered in some degree by the scientific community… if a test exists, you should use it.” Michael Kaback, medical geneticist

“as you move further and further away from an untreatable disease in which no one survives to cystic fibrosis and Gaucher’s disease, I find the application much more troubling and much less acceptable.” Mark Seigler, Ethicist, U. Chicago

“this is a moderate nightmare… this is a miniature but significant version of Big Brother…” Francis Collins, Director of the Center for Human Genome Research

1993 -- Why not expanding Dor Yeshorim to test for Cystic Fibrosis and Gaucher’s Disease – prevent marriages

Dor Yeshorim: expands testing to other, not invariably fatal, “Jewish genetic diseases” like Gaucher’s disease and Cystic Fibrosis

Nightmare or the Dream Of a New Era in Genetics?

By GINA KOLATA

In an ambitious attempt to eliminate common recessive diseases from their community, a group of Orthodox Jews in New York and Israel is using the most advanced molecular technology to screen young people considering marriage. Identification number. If a boy and girl want to date, or if they have already started dating, they are encouraged to call the New York Dor Yeshorim Central Office Hotline with their identification numbers. Then they are told either that...
A CLASH of GENETIC IDEALS

PREVENTION

Nightmare or the Dream Of a New Era in Genetics?

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In an ambitious attempt to replace faulty genes, researchers have already started screening young people for genetic disorders.

Using Genetic Tests, Ashkenazi Jews Vanquish a Disease

By GINA KOLATA

A number of years ago, five families in Brooklyn who had had babies... 

STIGMA OF TESTING? EUGENICS? A SUPPORTER OF DOR YESHORIM: “While ethicists agonize over some people’s being marginalized as marriage partners, they would do better to focus on the fact that medical conditions not manifesting themselves until middle age [like Gaucher’s disease] do not make them benign…. Prevention beats remedy any day.”

2003 – Testing for TSD hailed a success

Closing In on Cystic Fibrosis

Researchers are learning to replace a faulty gene...
1993-94: CF – HOPE FOR A CURE:

PREVENTING CF vs. THE DREAM of a CF CURE

Identification of Gene. Envisioning the replacement of faulty genes.

Closing in on CF Gene Therapy

GENE THERAPY – ADENOVIRUS VEHICLE “LEADING THE WAY”
CF Therapeutic Progress

- Sweat chloride test
- Antibiotics
- Lung transplant
- DNase (reduce respiratory infections, improve breathing)
Race and Genetics – how different cultures mediate issues of testing, prevention, treatment

1. RACE and Genetics – these controversies in the U.S. come in many varieties, and shifting forms – no single one-size-fits-all approach to avoiding controversy.
   - Testing, Prevention, Gene Therapy
   - Varies by group and within group, and by social context
   - Defined by progress, and ongoing controversies

2. CLINICAL DIFFERENCES IN DISEASE: shape how genetic innovations have been applied, and how they interact with ethnicity and social values (TSD 100% mortality, Gaucher’s disease, SCD)

3. WHO CONTROLS GENETIC TECHNOLOGY – shapes debate over race and genetics
   - Rabbis, Trusted Experts, Community, NCAA, federal government, outside experts to the community?

4. EXPERT and POPULAR DISCUSSION OVER RACE, CARRY MANY DIFFERENT MESSAGES:
   - the era of “personalized genomics” will transcend race
   - but some genetic differences are group specific (Caucasian disease, Jewish disease, black disease)