Technology, Diversity, and the Future of Health:
The Social Predicament of Genetic Innovation

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

What do the histories of these three diseases tell us

- genetic innovation amid social diversity
- technology’s impact on population health
- progress (genetic detection, prevention, testing, and treatment)
- cautionary warnings as we move from genetic testing… toward gene therapy and gene editing
TSD, SCD, and CF – COMMON FEATURES

1950s: Autosomal Recessive (established)
Mechanisms of Inheritance
(relationship of carriers → disorder)

1970s: Prevention via Genetic Testing/ Genetic Counseling

1950s-present: Identification of Cause leads to Hope for Technical Breakthroughs in Treatment

CARRIER PARENTS
25% CHANCE OF HAVING AFFECTED CHILD

THREE CAUTIONARY TALES
Genetic Progress amid Social Diversity

In each disease – genetic innovation has traveled different paths over decades, shaped by questions of race and ethnicity
1910 – SICKLE CELL FIRST CLINICAL DESCRIPTION (by James Herrick)

1940s - Dramatic impact of antibacterial agents (“a great masquerader”)

1950 – Linus Pauling discovery that a mis-substituted amino acid on the complex hemoglobin molecule caused sickling

CLINICAL VISIBILITY: Turned the disease from an obscure curiosity into the “first molecular disease”

1960s and 1970s: SOCIAL VISIBILITY AS A DISTINCTIVE BLACK EXPERIENCE. A “new” disease characterized by “pain and suffering among African-American that has been long ignored” – rising awareness resonated with political and cultural currents of the era
DIAGNOSTIC TECHNOLOGY and ANTIBIOTICS EXPAND CLINICAL VISIBILITY

Patients die from pulmonary disease, infection

Antibacterial agents in the 1950s and 1960s – become the leading edge of therapy. CF is unmasked as underlying disorder, causing infections

NEW THERAPIES MEAN PROGRESS AND NEW DANGERS, 1960s: “Any regimen of long-continued therapy with a single antibacterial agent invites the development of highly resistant organisms which may flourish in an environment rendered more favorable by the absence of susceptible bacteria.” New worries: Pseudomonas aeruginosa (Garrard, et.al)
1950s – SEARCH FOR “DE-SICKLING” AGENT:

One prediction 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.”

1970s -- Urea, promising desickling agent shows “no hematological of clinical benefit,” toxic side effects.

1990s – Hydroxyurea success (stimulates fetal hemoglobin, “genetic switch,” reduce painful crises, but not a cure)
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.”
BREAKTHROUGHS AND CONTROVERSIES

Genetic testing (counseling, persuasion, charges of ‘genocide’)

Bone Marrow Transplantation (cures, high risk for death from procedure, Graft-vs-Host disease)

Transfusion care (“living on borrowed blood”)

Pain care (“before you can get past the agony, you have to convince a doctor that it’s real”)

Access to care (insurance coverage, Medicaid)

Ethics of screening for trait in air force (1970s) college athletics (2012)
Sickle Cell Disease – Therapeutic Progress alongside Social Controversy

RISING LIFE EXPECTANCY
- Antibiotics
- Transfusion
- Prophylactic Penicillin
- Hydroxyurea (treatment of crises)

TAY-SACHS DISEASE – A DIFFERENT HISTORY OF SUCCESS AND CONTROVERSY

1880s: (Warren Tay and Bernard Sachs)

1930s: “almost exclusively observed among Hebrews”

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

1950s: Discovery and identification of the heterozygote (carrier)
- Identified as lipid storage disorder, lysosomal storage disease


HOPE FOR A CURE: 1971 -- “with detection and prevention of TSD possible, the question of cure arises…” Friedman

Widely seen as a “Jewish disease,” Carrier Frequency

1 in 25-30 Ashkenazi Jews
1 in 20 French Canadians/Louisiana Cajuns
1 in 200-300 U.S. population
AS HOPES FOR CURE FADE

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

URGENCY OF PREVENTION RISES – GENETIC TESTING OF CARRIERS TO AVOID BIRTHS:

ONE SOCIAL AND RELIGIOUS INNOVATION IN BROOKLYN, NY STIRS ADMIRATION AND CONTROVERSY

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

FOR ULTRA-ORTHODOX JEWISH GROUPS, ban against abortion, search for other options

Rabbi’s Innovation: CHEVRAH DOR YESHORIM “GENERATION OF THE RIGHTEOUS” Testing Adolescents for Carrier Status – Arranged Marriages to avoid producing TSD, PRACTICE SPREADS
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

Expands testing to other, not invariably fatal, “Jewish genetic diseases” (high prevalence)
UPWARD TRENDS IN CYSTIC FIBROSIS

- Sweat chloride test
- Antibiotics
- Lung transplant
- DNase (reduce respiratory infections, improve breathing)

WHY THE CONTROVERSY OVER THIS INNOVATION IN CF PREVENTION?
A CLASH of GENETIC IDEALS

PREVENTION ... vs. DREAMS OF A CURE?

Nightmare or the Dream Of a New Era in Genetics?

By GINA KOLATA

In an ambitious attempt to identification number. If a boy eliminate common recessive diseases from their community, a group of Orthodox York and Israel is advanced molecule to screen young parenthood.

Using Genetic Tests, Ashkenazi Jews Vanquish a Disease

By GINA KOLATA

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

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
1990s – Which genetic future to pursue amid social diversity?

The dream of curing CF (following identification of gene) and visions of “replacing the faulty gene”? Or the ideal of prevention?

IDENTITY: Who has the right to define the future uses and misuses of genetic interventions? (Is CF a “Caucasian disease”? Or a “Jewish disease”?)
THE SOCIAL PREDICAMENT OF GENETIC INNOVATION – TECHNOLOGY, DIVERSITY, AND THE FUTURE OF HEALTH

1. NEW CHALLENGES FOLLOW TRANSFORMATION OF ACUTE DISEASES INTO CHRONIC DISEASES – new clinical management with rising life expectancy

2. COPING WITH MEDICAL, ETHICAL, AND SOCIAL CHALLENGES CAUSED BY TECHNOLOGIES THEMSELVES

- Genetic testing (disease detection but also stigma, discrimination, use and misuse)
- Bone Marrow Transplantation (cure, mortality due to procedure, or Graft-Versus-Host disease)
- Pain medicine (access: convincing a doctor it is real, and relief is deserved)
- Gene editing and gene therapy (Crizanlizumab) Risk of insertional oncogenesis

“Little would be gained by sickle cell disease patients if they merely traded the mortality associated with the primary disorder for a new set of disabling symptoms resulting from their treatment.” (Beutler, 1991)
3. TRANSLATING TECHNOLOGICAL INNOVATION INTO BETTER HEALTH WILL HINGE ON:

WHO CONTROLS THE USE OF TECHNOLOGIES?

WHICH POPULATIONS WILL BENEFIT?

HOW GENETIC INNOVATION RELATES TO GROUP IDENTITY AND WELL-BEING IN A DIVERSE U.S. AND WORLD?

HOW SOCIETY MANAGES ACCESS?

WHETHER WE CAN ANTICIPATE, AND MANAGE, THE USES AND MISUSES OF TECHNOLOGY?

WHETHER WE CAN FOCUS ON FUNDAMENTALS OF CARE EVEN AMID THE HYPE…