CARRIER SCREENING:
POPULATION DIFFERENCES, STIGMA,
AND THE SPECTER OF EUGENICS

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RESEARCH SUPPORTED BY: ETHICAL, LEGAL, AND SOCIAL ISSUES (ELSI) PROGRAM, NHGRI; and THE JAMES S. MCDONNELL FOUNDATION
Lessons of the Past:

• Balancing the screening interests of individuals, communities, and society? The importance of historical sensitivity and cultural competence among health practitioners who engage in screening.

• How to target screening to distinct populations? The challenge of “hidden” versus obvious subpopulations. One-size does not fit all; how screening relates to group values and concerns.

• In health care, knowing when screening is not the answer for some populations. Other goals: treatment and extension of life, relief. The importance of competent screening programs among populations whose group identities are invested in the maintenance of values that are distinctively different than that of the majority culture.

TODAY: ONE HISTORICAL CASE STUDY (TAY-SACHS DISEASE), WITH SICKLE CELL DISEASE AND CYSTIC FIBROSIS AS BACKDROP.
CONTROVERSIES in CARRIER SCREENING, STIGMATIZATION, AND POPULATION – the case of sickle cell disease

• LINUS PAULING 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... It 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.” UCLA Law Review

• AIR FORCE POLICY ON TRAIT CARRIERS (1970s); UREA DEBACLE AND SEARCH FOR DESICKLING AGENTS

• Hydroxurea; Pain Management (80s/90s); Prophylactic Penicillin
TSD, SCD, and CF: Linked Historically

Autosomal Recessive (established in 1950s)

Molecular Mechanisms and Mechanisms of Inheritance Explained (1960s)

Possibilities of Prevention via Genetic Testing/Counseling (1970s)


> Each disease -- linked to questions of race and ethnicity; the term “genetic disease” does not do full justice to their complexities
The Tay-Sach’s Historical Trajectory (Warren Tay and Bernard Sachs)

1880s -- ORIGINS AS “JEWISH AMAUROTIC 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.

TECHNOLOGICAL DEVELOPMENTS AT MID-CENTURY – transform screening/prevention possibilities

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

1969: O’Brien and Okada – deficiency of hexosaminidase A (hex A) which results in buildup of lysosomes in brain tissue. 1971 -- “with detection and prevention of TSD possible, the question of cure arises…” Friedman

THERAPEUTIC OPTIMISM: 1975 -- “we are entering a new phase in the treatment of genetic disease -- therapy by replacement of the deficient enzyme” (Roscoe Brady)
BY 1982 -- ENZYMATIC REPLACEMENT IN TSD DEEMED A FAILURE

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

DEEPLY INTERTWINED WITH JEWISH IDENTITY

-- Theories about TSD (balance polymorphism?)
-- Evolutionary adaptation to Jewish ghetto and TB??
-- Heterozygote resistance??
-- Mate selection?? (Rabbis marital choices)

> Despite its prevalence also among: French-Canadians, Catholic Franco-Canadians in NH, Louisiana Cajuns
A BREAKTHROUGH IN PREVENTION? A dramatic SUCCESS STORY of modern genetics emerges – TESTING SERVING THE NEEDS of ethnic/religious community

Into 1971-75: SCREENING COUPLES, COUNSELING, THERAPEUTIC ABORTION

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

FOR ULTRA-ORTHODOX JEWISH, proscription against abortion limits options

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”
By the early 1970s, a wide range of techniques available for preventing the birth of Tay-Sachs babies. Where prenatal testing available, many Americans chose to abort TSD fetuses. Carriers may choose not to have children. For these and other reasons, the results since the 1970s have been dramatic: a gradual decline of TSD among Jews living in the United States, and in many communities even its total eradication. In a relatively short time, TSD had been transformed into a modern genetic success story.

One of the major factors in the success of prevention has been the role of rabbis, religious leaders, and scientists in developing innovative techniques to spread information about the disease.

“I went knocking on the doors of community leaders, rabbis, anyone who would listen to me and some of those who weren’t, telling them that this was a problem and we had to do something about it. The point I made was that this was a problem for the entire community, not just for me…” -- Rabbi Josef Ekstein, founder Dor Yeshorim
“It is the obligation of every parent, without exception, to turn to the Dor Yeshorim and heed their advice, before finalizing a match for his or her child.”

The goal: “to eliminate Tay-Sachs from the Orthodox community, and to do it in accordance with strict Jewish law.”

“If a peek into a prospective couple’s genetic code shows a bad match, they are discouraged from even dating and certainly from marrying.”

“an adolescent rite of passage”

“Every year, Dor Yeshorim representatives go to the private high schools where many Orthodox families send their children… Those tested are given a six digit identification number. If a boy and girl want to date, or if they have already started dating, they are encouraged to all the New York Dor Yeshorim Central Home Office with their identification numbers. Then they are told either that the match is compatible – that they are not at risk of having children with the disease in question – or that they each carry a recessive gene that could result in a child with the diseases.”
A SUCCESSFUL EFFORT IN CARRIER SCREENING: The Chevrah Dor Yeshorim in broader context

• Ultra-Orthodox proscription against abortion

• Role of rabbi in family and marital decision-making, prevention of suffering (of parents)

• American Jewish concerns about group survival, shrinking birth rate, intermarriage (1970s-1980s)

Interruption of Reproduction

“the spiraling rate of intermarriage between Jews and non-Jews… could seriously diminish the American Jewish community, according to a study… by the American Jewish Committee”

The shrinking birth rate is a concern.

CONTEMPORARY couples grapple with a complex set of personal considerations when they tackle the decision to become parents. For Jewish couples, there is an additional imperative: their sense of obligation to halt the decline in population that demographers say poses a threat to the survival of Judaism in this country.

Two conferences designed to confront this issue were scheduled for this week. Representatives of 28 major Jewish groups, including the rabbinical associations for the Orthodox, Conservative, Reform and Reconstructionist branches of the faith, along with such diverse groups as B’nai B’rith International, Hadassah, the American Jewish Congress and the Women’s Branch of the Union of Orthodox Jewish Congregations, met at the offices of the American Jewish Committee in Manhattan on Monday and Tuesday. Their meeting, entitled the National Conference on Jewish Population Growth, produced

THE SPIRALING RATE OF INTERMARRIAGE BETWEEN JEWS AND NON-JEWS… COULD SERIOUSLY DIMINISH THE AMERICAN JEWISH COMMUNITY, ACCORDING TO A STUDY… BY THE AMERICAN JEWISH COMMITTEE”

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CARRIER SCREENING: 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
EARLY 1990s – CONFLICTING GENETIC IDEALS

PREVENTION OF GENETIC DISEASE

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

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

Weighed against rising life chances and hope of cure… Francis Collins sees Dor Yeshorim for CF as “moderate nightmare”

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.”
1930s -- DOROTHY ANDERSON....
Cystic fibrosis of the pancreas: “severe malabsorption potentially treatable by dietary supplements and nutritional management.”

50s and 60s: FROM PANCREATIC INSUFFICIENCY to generalized disorder

“In light of the ‘newness’ of the disease, it is understandable that those who are studying it and caring for patients should not be in full agreement on all its aspects.” (Kenneth Landauer, Guide to Diagnosis… Management of CF, 1963)

1965 -- Paul di’Sante Agnese notes sweat electrolytes elevated in CF patients… “most eventually die in childhood, adolescence, or young adulthood, of the chronic pulmonary involvement which usually dominates the clinical picture… despite its name, so-called cystic fibrosis of the pancreas is in reality a generalized disorder.”

“In patients with CF there is a ready-made experimental model in which to study the interaction of mucopolysaccharides and electrolytes.”
Making CF visible: The impact of the ANTIBACTERIAL REVOLUTION

Trajectory – 50s/60s
“CF is an elusive simulator of other diseases…”

Patients dies from …
Pulmonary disease
Infection

Antibacterial agents in the 1950s and 1960s -- the leading edge of therapy

More patients being diagnosed and treated (parallels SCD story) – a panethnic disease?

BUT ALSO… advent of the antibacterials transforms nature of the disease…
1951: “the enlarged chemical and antibiotic armamentarium of the physician today has brought increasing clinical importance to the Pseudomonas strain of organisms at all ages.” (Garrard, et.al.)
THE AGE OF ANTIBIOTICS AND THE POPULATION OF CF PATIENTS – research and patient care

• UNMASKED “The great masquerader”

• TRANSFORMING the clinical reality of disease (acute disease into a chronic one)

ADVANCES IN THERAPY AND RESEARCH CREATE NEW PROBLEMS… LOOKING INTO THE FUTURE FROM 1951

“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.” (Garrard, et.al)

1968: “There is little doubt that the establishment of this species [Pseudomonas aeruginosa] in the respiratory tract is encouraged by suppression of other bacteria by antibiotics” (Burns and May, 1968)
BY 1980s... THE IMPACT OF DRUG REVOLUTION ON CF

- RISING LIFE EXPECTANCY – CF TRAJECTORY
- RISING EXPECTATIONS
- NEW FRUSTRATIONS
- POPULATION — “most common lethal genetic disease among Caucasian Americans”

PATIENTS GROWING OLDER: “the median survival age in 1989 was 26 years, compared to only 7 years in 1964. The extended survival is due in part to more aggressive treatment of pulmonary disease and malnutrition…” W.H. Frist, 1991 (article on Heart-Lung transplant)

RESEARCH, SUBJECTS, INNOVATION, 1985: “Historically, patients with CF have been given a variety of prophylactic regimens. It was common at one time to give tetracycline for a few months, then chloramphenicol for a few months, and then other drugs for a few months… Perhaps when the basic defect is understood, the relationship of the host to the microorganism will be better understood.” (Nelson)
1993/4: EXPANDING THE DOR YESHORIM TO TEST FOR AND PREVENT CF RUNS CONTRARY TO THE DREAM of a CURE

Identification of Gene.
Envisioning the replacement of faulty genes.

Closing in on CF Gene Therapy

GENE THERAPY – ADENOVIRUS VEHICLE “LEADING THE WAY”

A NEW REVOLUTION?
Problems mount in adenoviruses used in “patients”…

“When administered in low concentration [adenovirus] ineffective, at high doses causes acute inflammation…”

Experiments halted in CF… Crystal: GenVec “now concentrating on gene therapy for cardiovascular disease…” “Maybe the quickest route to solving cystic fibrosis is to take a detour” – Genzyme executive

MAJOR CRISIS OF GENE THERAPY

POSITIVE SPIN: 1995: “This commercial pressure may also account for some of the hype surrounding developments in gene therapy… If you’re the leader of a gene-therapy company… ‘you try to put as positive a spin as you can on every step of the research process… because you have to create promise out of what you have -- that’s your value.” James Q. Wilson, Inst for GT, Penn
DILEMMAS IN CARRIER SCREENING: Should the Dor Yeshorim be extended to CF testing and prevention? A clash of conflicting ideals, values, and histories

(Jewish Orthodox community health and preservation) AND (The Question for a Genetic Cure)

EACH GENETIC DISEASE AND EACH POPULATION follows a UNIQUE TRAJECTORY: shaped by complex interaction of science, technology, medicine with values, subculture and society

Histories of therapeutic advancement – solving some problems, creating others in their wake

Different interests and social, political, economic investments in screening
Sickle Cell Disease – shares history with both CF and TSD

• Dramatic impact of antibacterial agents (great masquerader)

• Clinical description early in the century (James B. Herrick)

• Molecular Understanding and Inheritance Illuminated at mid century – Linus Pauling and J.V. Neel

Autosomal Recessive

THREE DISEASES TRAVELING DIFFERENCE HISTORICAL TRAJECTORIES:

DIFFERENT KINDS OF STIGMA, DIFFERENT MEANINGS FOR EACH POPULATION, AND CARRIER SCREENING COMES TO HAVE A DIFFERENT POLITICAL, SOCIAL, AND CULTURAL MEANING

TSD: PREVENTING CERTAIN DEATH AND SUFFERING...
CONTROVERSIES in CARRIER SCREENING, STIGMATIZATION, AND POPULATION – the case of sickle cell disease

• LINUS PAULING 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.” UCLA Law Review

• AIR FORCE POLICY ON TRAIT CARRIERS (1970s); UREA DEBACLE AND SEARCH FOR DESICKLING AGENTS

• Hydroxurea; Pain Management (80s/90s); Prophylactic Penicillin
HYDROXYUREA – “genetic switch”; PROPHYLACTIC PENICILLIN

“I don’t like the word breakthrough… But we can now show that this drug therapy can make a difference.” (Reid, 1986)

BONE MARROW TRANSPLANT (peril and promise)

(high-risk, high-gain intervention – Cure/Graft-vs-Host-Disease/Death from Procedure):

“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)
CONCLUDING COMMENTS – TSD, CF, SCD CARRIER SCREENING

1. CONFLICTING cultural values over DISEASE, and the best way to combat disease… (e.g., prevention or cure), and divergent cultural views of genetic medicine

2. All “genetic diseases” or heritable disorders considered in their own terms. “Genetic” or “Hereditary” disease, as a label, does not do justice to their complex, divergent trajectories and cultural meanings

3. LESSONS of the PAST: The Ethics of the DOR YESHORIM AND CF (right for Ultra-Orthodox…)

Lessons of the Past:
• Balancing the screening interests of individuals, communities, and society? Historical sensitivity to values, and cultural competence among health practitioners who engage in screening

• How to target screening to “hidden” and obvious subpopulations? One-size will not fit all

• When screening is not the answer. Other goals: treatment, relief, longevity? Competent screening programs among populations whose group identities are invested in the maintenance of values that are distinctively different than that of the majority culture