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BABIES' BLOOD: FRAGMENTATION, REDEMPTION, AND PHENYLKETONURIA

M. SUSAN LINDEE*

In a ten-year period, from 1955 to 1965, an obscure metabolic disorder emerged from the medical ghetto of genetic disease to become the biochemical center of a vast network of information, technology, social management, and legislation. Phenylketonuria ("PKU"), a rare disorder of phenylalanine metabolism, became the focus of a major public health initiative. Present in approximately 1 in 15,000 American births, PKU attracted the funding and interest of national organizations devoted to the control of mental retardation in children. Dozens of scientific papers appeared documenting the course and treatment of PKU; the U.S. Children's Bureau sponsored a field trial of a new diagnostic test; and by September 1965 thirty-two state legislatures established neonatal PKU screening as public health policy. Screening was mandatory in twenty-five of these states. Thus in a short period, a rare genetic disease came to be embedded in a dispersed system of medical and political management.

Explanations of these events have appeared in retrospectives by participants, in scientific reviews, and in scholarly studies by ethicists, political scientists, and historians. Perhaps the simplest narrative

* Associate Professor, Department of History and Sociology of Science, University of Pennsylvania. I owe special thanks to archivists Daniel Barbiero at the National Academy of Sciences, Tab Lewis at the National Archives and Records Administration at College Park, Maryland, and Matt Fulgham at the National Archives and Records Administration I in Washington, D.C. Marion Robertson, neither an archivist nor historian, thought it was important to save old records and because she thought so, I was able to work with Maryland Department of Health records that were "archived" in an unused cabinet in Baltimore. For their insights, I am grateful to Robbie Aronowitz, Scott Gilbert, Barbara Kimmelman, Dorothy Nelkin and Diane Paul. My research for this project has been funded by the Burroughs Wellcome Fund 40th Anniversary Award.

1. For a description of the field trials, see ROBERT GUTHRIE & STEWART WHITNEY, U.S. CHILDREN'S BUREAU, PUB. NO. 419, PHENYLKETONURIA DETECTION IN THE NEWBORN INFANT AS A ROUTINE HOSPITAL PROCEDURE (1964) (on file with the U.S. Children's Bureau, National Archives and Records Administration, Washington, D.C.) [hereinafter CHILDREN'S BUREAU, PUB. NO. 419].


3. For a perceptive overview of these events and their policy implications, see Diane B. Paul,
portrays the rise of PKU screening as the strict consequence of advancing knowledge. Scientists began to understand how to intervene in PKU, and this understanding mandated a legislative and public health program. PKU screening was therefore the natural consequence of new knowledge.4

A somewhat more complicated story appeared in a 1975 National Academy of Sciences report prepared by a committee of the American Society of Human Genetics.5 In this account, PKU screening programs derived not from knowledge but from ignorance, specifically "fragmented, uneducated and hurried decision-making."6 State legislators, swayed by emotional pleas from parents of mentally retarded children and by "unfounded claims" about the efficacy of a low-phenylalanine diet, rapidly implemented a vast public health system without considering the consequences. The report noted that "[t]here was very little recognition of the implications for public policy, or for the impact on individuals who were screened, of the fact that PKU is a genetic disease."7

These narratives explaining how PKU became a public health priority are compelling ways of situating a genetic disease that has had a high political profile. Yet I do not adopt either perspective here. Instead, I tell the story of the rise of the political control of PKU without placing knowledge (its presence or its absence) in the center, focusing rather on the labor involved in the collection,
analysis, and management of blood.

I suggest that blood directly brings the individual physically into the network of testing and rationality that is central to contemporary biomedicine. The management of babies' blood is a laboratory replication of the social management of PKU. It is a controlled, choreographed re-enactment of a larger political drama. More broadly, I suggest that the systems of organization, manipulation, and control that make human bodily materials (extracted tumors, autopsied remains, and blood) effective or benevolent medical resources also make manifest the relationships of these materials to political power.

A large body of scholarly literature explores the political meaning of scientific knowledge in relation to bodily difference, pathology, race, illness, gender, and class. Such studies emphasize the roles of theory, culture, or ideology in scientific interpretations of the body. I here suggest another approach. I attend to a laboratory technique central to mandatory state testing of newborns and explore the clinical protocols, practices, and interpretive uncertainties surrounding a particular bodily material—namely, babies' blood. I focus on the physical process of the management of newborns' blood and propose that attending to such processes illuminates the many layers of work involved in making PKU—and by inference genetic disease in general—into a compelling public health problem. By following the state's management of newborn blood, I draw links between the physical and ideological labor that constructed this genetic disease as a public priority.

I further suggest that this labor created a system into which other diseases could be readily incorporated, though these diseases had to share certain properties with PKU: genetic, metabolic, and present in a newborn's blood. By the time the assumptions guiding the political embrace of PKU came to be questioned in the mid-1960s, the system of blood collection and analysis that PKU made possible persisted unaffected, acquiring new properties, new advocates, new diseases, and new purposes.

8. This is a fairly diverse literature. See, e.g., Anne Fausto-Sterling, Myths of Gender: Biological Theories about Women and Men (1985); Sander L. Gilman, Difference and Pathology: Stereotypes of Sexuality, Race, and Madness (1985); Sander L. Gilman, Disease and Representation: Images of Illness from Madness to AIDS (1988); Thomas Laqueur, Making Sex: Body and Gender from the Greeks to Freud (1990); Londa Schiebinger, Nature's Body: Gender in the Making of Modern Science (1993).

9. For a useful exploration of the contemporary state of neonatal testing, see Committee on
My interest in such matters is a consequence of a reading of Carolyn Bynum on ideas about material continuity and personal survival in thirteenth and fourteenth century theological debates. Bynum proposes that by considering the management of bodily materials—by examining what contemporaries believed about where and how relics should be handled—one could gain insight into larger questions of the place and meaning of the body in Western thought. Her work provoked me to think about how fragmented bodies acquire meaning and about the cultural context that makes a piece of a human body a sacred object or a piece of data, to be stored in a crystal reliquary or in a state-sanctioned laboratory, “preserved” and immortal as a consequence of divine intervention or the long-term storage of Guthrie cards.

I. THE BLOOD

PKU was identified as a familial disorder of phenylalanine metabolism in 1934 by Asbjorn Folling, a physician whose family included several children who had the disease. He was prodded by a mother who wanted to understand her children’s mental retardation and their peculiar odor. Folling found that the children’s urine turned green upon the addition of ferric chloride and determined that this color was a consequence of the presence of phenylpyruvic acid in the urine.

British geneticist Lionel Penrose soon suggested that a diet low in phenylalanine might be an effective therapy for PKU. This was interpreted at the time as too expensive and impractical. In 1951, two British biochemists tested a controlled diet on three young children—not newborns—and reported some improvement. By 1955, two other groups of researchers had tried low-phenylalanine...
diets in affected children with some reports of success. Horst Bickel, a physician in England, reported that a three-year-old girl he was treating stopped having convulsions. Bickel proposed that if the diet had begun earlier mental retardation might have been avoided.14

The possibility of therapy and cure that this dietary intervention promised was apparently intoxicating. A patchwork of British screening programs, using urine testing for phenylpyruvic acid, was in place by 1959, though this screening resulted not from legislative action but from local decisions by Public Health Department officials.15 The testing was facilitated by the standard British practice of home visits to young infants. Phenistix, the available urine test, was most reliable when used with infants six to eight weeks of age, and infants in Britain were routinely seen by a health professional in their homes at about this age.16 In contrast, most newborns in the United States left the hospital after two or three days—too early for an effective urine test—and home visits were not a part of American medical care. Therefore, in the United States a different bodily fluid would better conform to existing medical practice.

Blood was to become the material sign of hidden metabolic disease. It was the transferable, mobile, testable segment of a new body that could be integrated into the American public health system. It was the currency of the emerging field of public health genetics, the commodity that health departments generated (by ordering its removal from all newborns) just as they generated information and clinical practices.

When Robert Guthrie and his laboratory assistant Ada Susi developed a test that could detect the presence of excess phenylalanine in a newborn’s blood, they provided the technological frame for a massive blood collection program. There was an interaction between bodily fluids and health care delivery systems. A blood test became central to the American system due not only to Guthrie’s ingenuity but also to the prevailing practices of infant care in the United States. The test itself was modeled to meet an existing space, and then in occupying that space it made possible other kinds of tests that drew on the bodily fluid the test routinely produced.

15. See James W. Farquhar et al., Problems of Routine Screening for Phenylketonuria, 2 LANCET 498 (1962), for a description of one such local screening program.
16. See id. at 498.
Ultimately, the Guthrie test helped to create the legislative frame that redefined PKU and eventually public health genetics.

Guthrie’s full description of this test appeared in September 1963 in *Pediatrics*,¹⁷ though Guthrie had proposed the use of a similar inhibition assay in the detection of metabolic disorders a year earlier at a conference.¹⁸ His new blood test was an indirect test that calculated levels of phenylalanine based on bacterial growth under specialized conditions. A strain of bacillus subtilis, a ubiquitous soil bacteria not pathogenic to either animals or humans, was mixed with an agent inhibitor that normally stopped its growth. To this mixture was then added a punch-hole of the blood-soaked filter paper collected from the newborn’s heel. If the phenylalanine was present in the blood, it would affect the ability of the inhibitor to stop the bacterial growth. Thus, if the blood counteracted the inhibitor and the bacteria grew, the test for phenylalanine was positive. The size of the halo of bacterial growth was taken as a quantitative sign of the level of phenylalanine. Technicians then interpreted the visual phenomenon in numerical terms.

Although the procedure was not inherently difficult, at every step it was possible to invalidate the test in some way—by timing the test too early in the baby’s life, inadequately soaking blood through the filter paper, mislabeling a sample, failing to autoclave properly, or misinterpreting the “semi-quantitative” results (the halo). Guthrie himself emphasized the importance of the process of taking blood, stressing that the blood should be applied “immediately to [the] . . . very absorbent filter paper.”¹⁹ He also advised that the spot of blood after air drying “should be at least 3/8 inch in diameter (but not more than 1/2 inch) and close enough to the edge of the paper” so that a disk could be easily punched out of it.²⁰

Technicians and medical staff responsible for the test were provided with instructions for obtaining blood specimens which told them to set up a “well lighted work area” and to “wash hands.”²¹

   ¹⁹. Guthrie & Susi, supra note 17, at 338.
   ²⁰. Id.
   ²¹. Memorandum from William J. Peebles, M.D., Commissioner of Maryland Department of
These instructions assumed that the parent would be present and involved in the test, as evidenced by the suggestion that the parent hold the infant "in [a] prone position on lap or table with heel or toe lower than body."\textsuperscript{22} The technician then had to choose an "area for puncture"—usually the heel—and "incise deeply enough to produce free flow of blood."\textsuperscript{23} Subsequently, the technician had to "hold [a] Form BL50 with printed circles uppermost . . . until each circle [was] completely filled" with blood.\textsuperscript{24} Guthrie noted that the paper was so absorbent that "even very viscous blood from a young infant spreads through the paper, so that the appearance of the blood spot is similar on both sides of the paper."\textsuperscript{25} In any case, these conditions had to be met in order to obtain a uniform blood sample in the paper punch.

The test was choreographed—the infant's and mother’s position and the wound's proper bodily location specified. Every action of those involved in this process, which violated the bodily integrity of the newborn, was subject to standardization and technical control. Guthrie constructed the process of extraction as a social drama relevant to the state’s interest in his test. Technicians needed to see the explicit relationship between blood, properly distributed on the filter paper, and the political legitimacy of the test.

Guthrie's emphasis on soaking the filter paper through completely—so that when dried the circles of blood would appear the same on the back and front—reflected persistent difficulties with this task. In Maryland, an insufficient quantity of blood collected on filter papers created a backlog of second tests early in the program.\textsuperscript{26} “Reliable analysis” depended on filling the three-eighths inch circle entirely and "repeated failure to do this" made repeat tests necessary.\textsuperscript{27} Furthermore, "[i]nvestigation of the reasons for this problem, [showed] that it [occurred] most frequently where personnel...

\textsuperscript{22} Id.
\textsuperscript{23} Id.
\textsuperscript{24} Id.
\textsuperscript{25} Guthrie & Susie, supra note 17, at 338.
\textsuperscript{26} See Memorandum from William J. Peebles, M.D., Commissioner of Maryland Department of Health, to Hospital Administrators, Maryland Department of Health, Progress Report No. 8: Guthrie Screening Program for PKU (Nov. 3, 1965) (on file with Maryland Department of Health, Baltimore, Md.).
\textsuperscript{27} Id.
in the newborn nursery [were] rotated or changed.\textsuperscript{28} Thus, even at this first step—at the point of extraction by a standardized procedure—the workplace culture (rotation of personnel) interacted with the intractability of the newborn body (its tendency to be uncooperative, squirmy, and difficult) and the qualities of the blood itself (extremely viscous) to shape the utility of the test.

In the next step, the control of mechanical things (autoclaves and paper disks) replaced the control of social interaction (technician, infant, and mother). The spots of blood on the Guthrie cards were numbered with a pencil, and the cards were placed on pieces of metal screening or wire test tube racks to be autoclaved (heated) at fifteen pounds pressure for three minutes with dry steam.\textsuperscript{29} This prevented blood pigments from later diffusing from the paper disks into the agar during incubation, a diffusion which tended to mask possible growth zones. Prolonged autoclaving, however, would destroy the phenylalanine. A one-fourth inch in diameter disk then was punched from the center of the blood spot, and the disks placed in rows on a clean piece of paper in the same sequence that they were placed on the agar for assay.\textsuperscript{30}

These paper disks were processed, yet unread, signs of invisible disease and the presence of the disease could be obscured by the blood itself; blood diffusing into the agar; autoclaving, if carried out too long; or mislabeling, resulting in allocation of the blood to the incorrect body. Moreover, a 1963 survey suggested that the most difficult step for many technicians was the quantitative interpretation of the halo of bacterial growth.\textsuperscript{31} Thus, newborn blood was not a transparent sign of a disease or a direct guide to state control, but a sign mediated by the labor of technicians who varied in their laboratory skills.

The Guthrie test made PKU a disorder that could be completely present in the newborn infant. Formerly diagnosable in the toddler

\textsuperscript{28} Id.
\textsuperscript{29} See Guthrie \& Susi, \textit{supra} note 17, at 338.
\textsuperscript{30} See id.
\textsuperscript{31} See Gladys Krueger, Remarks at the Division of Health Services Staff Meeting, \textit{Assessment of Performance of Laboratories Participating in a Trial of Phenylalanine Screening Method} (June 6, 1963) (transcript available at the U.S. Children's Bureau, National Archives and Records Administration, College Park, Md.). This survey, conducted by the U.S. Children's Bureau which managed the initial field trials of the Guthrie test in the United States, found that laboratories varied in their skill levels and that the test seemed to be particularly prone to false negatives, a type of error that could undermine its value as a screening tool. See id.
through a suite of symptoms or in the eight-week-old infant with a urine test, the disease came to potentially exist in the body of the newborn as early as seventy-two hours after birth with the Guthrie test. The timing of diagnosis of any disease is always important, but in the case of genetic disease timing is particularly dramatic. For example, the technologies that make it possible to identify Huntington Disease in a fetus change the meaning of the disease for everyone involved. PKU was an early case in which a genetic disease could be made present—not in this case through DNA testing, but through biochemical manipulation of blood—before it was a clinical syndrome.

This test also indirectly led to a definition of PKU as a racial disease—a disease of the blood in the traditional sense. It was not that those involved believed that African-American babies could not have PKU, but rather that including African-American babies in the initial field trials would make the test appear less cost-effective as a public health screening tool. This need to legitimate the blood test as an appropriate guide to state intervention provoked a particular way of thinking about PKU.32

II. A RACIAL DISEASE

When Guthrie proposed the field trial to the Children's Bureau on May 2, 1962, he simply stated, "It is suggested also that nonwhite infants should not be included in this study."33 This was one of the limitations on the study. Other limitations included a suggestion that the trial take place only in hospitals in which "blood specimens can be collected as late as the third or fourth day of life."34 A few weeks later the Children's Bureau sent out a letter to states invited to participate in the field trial. Among the "points [which] should be read carefully" was the following:

32. Penrose had earlier suggested that the disease had a racial component, though with a very different intent. In his 1946 paper in The Lancet, he emphasized its apparent absence in Jews in an effort to make an antiracist point about racial groups and their susceptibility to disease. See L.S. Penrose, Phenylketonuria: A Problem in Eugenics, 1 LANCET 949 (1946). I am grateful to Diane Paul for pointing out this reference to me. On more general questions of race and disease, see Keith Wailoo, Drawing Blood: Technology and Disease Identity in Twentieth-Century America (1997).


34. Id.
The plan provides that the infant population used for this initial trial should consist of white infants who are three or four days of age (because phenylketonuria is virtually non-existent in non-white groups and because of our lack of knowledge as to what phenylalanine levels are in the first four days). Hospitals selected, therefore, should be chiefly those who serve white infants and who discharge such newborn infants only after three or four days.35

Two sorts of ignorance therefore shaped this initial field trial: ignorance about the disease's racial distribution and ignorance about its manifestation in the first seventy-two hours of life. But the category "nonwhite" was much more ambiguous than the category "infants at least three or four days old," as one regional medical director pointed out.

Lucille J. Marsh, a physician in charge of the Children's Bureau office in Chicago, questioned the decision to exclude nonwhite infants. "This seems to me a mistake," she said, "even though cases are rarely found in non-white infants according to our present knowledge."36 She regarded "some information as to the screening results among non-white infants" as valuable.37 She also suggested that there was "presently so much confusion as to the percentage of white or non-white blood in many population groups as, for example, in the large Negro population, the Porto [sic] Ricans, the Mexicans, etc., that the division into white and non-white will probably be purely arbitrary in the next generation."38 The impurities of blood in the American melting pot, her argument proposed, negated its potential role as a border between productive and nonproductive bodies.
A staff member at the Children's Bureau responded with the argument that nonwhite infants would skew the sample. The Bureau was concerned about "getting an adequate sample of white infants where the expected incidence is approximately 1 in 20,000." Because there was only one reported case of PKU in a nonwhite infant, the Bureau feared that "over half of the infants included might be nonwhite and this . . . could lead to the mistaken conclusion that this assay is not effective as a screening tool." Therefore, the exclusion of nonwhites was necessary in order "to give the assay a fair trial with a group where at least we have a vague idea of incidence."

The efficient management of the Guthrie test called for restricting its use to a racial and political category—an infant body (white) marked as productive. The blood of nonwhite infants was a public resource irrelevant to the Children's Bureau's promotion of the Guthrie test. So when a Civil Rights Commission official learned of the policy and complained, the Children's Bureau staff framed the exclusion as efficient resource management.

By constructing their screening trial around a population they believed to be at higher risk for the condition and thereby excluding

39. Letter from Rudolf P. Hormuth, Specialist in Services for Mentally Retarded Children, U.S. Children's Bureau, to Lucille J. Marsh, M.D. (June 6, 1962) (on file with the U.S. Children's Bureau, National Archives and Records Administration, College Park, Md.). Hormuth acknowledged that there might be some cases of PKU among the nonwhite population but stated that so far "existing screening and diagnostic methods have not turned up many cases." Id. In response to the suggestion that nonwhite infants might have elevated blood phenylalanine without having PKU, Hormuth commented that the Children's Bureau would be "interested in exploring" the question, but only as a separate project—not as a part of the initial screening trial of 400,000 infants to assess the Guthrie test. See id. If "some states are interested in exploring phenylalanine levels in nonwhite infants (in addition to doing their share of white infants for the field trial)," he indicated the possibility of arranging this with Guthrie, who distributed the test kits. Id. He advised that it would be important, however, to "keep these figures separately. Urine screening of negro infants in well baby clinics thus far has not been productive." Id.

40. Id.

41. Id.

42. The complaint came in April 1963 when Mrs. Martin of the U.S. Commission on Civil Rights telephoned to ask if the PKU program was sponsored by the Children's Bureau and if the government was contributing funding. The Commission had a complaint from Springfield, Massachusetts, stating that nonwhite children were not being included in this program. In practice in participating hospitals, Massachusetts was apparently screening all infants—white and nonwhite—and was about to approve legislation requiring that all newborns be screened in all hospitals. Hormuth responded that the case that Martin referred to in Springfield, Massachusetts, was probably unrelated to the Children's Bureau program as it did not involve a newborn. See Memorandum from Rudolph P. Hormuth, Specialist in Services for Mentally Retarded Children, U.S. Children's Bureau, to Ruby G. Martin, Staff Attorney, U.S. Civil Rights Commission, Exclusion of Non-white Children from PKU Screening Program (Springfield, Massachusetts) (Apr. 11, 1963) (on file with the U.S. Children's Bureau, National Archives and Records Administration, College Park, Md.).
nonwhite infants, Guthrie and the Children's Bureau staff constructed PKU as a racial disease. They amalgamated categories—"white" versus "nonwhite" babies—in ways that reflected their institutional concerns over justifying the Guthrie test as a mass screening technology. My point is not that the exclusion of "nonwhite infants" was malicious. In the context of this field trial, the decision to construct PKU in racial terms made sense. But the case does demonstrate how particular ways of managing bodily materials—in this case a test of phenylalanine in newborns' blood—can provoke limited ways of thinking about a disease and limited ways of making public policy.

Marsh was right to point out that rates of PKU in nonwhite populations were unknown. Under these conditions, a "fair trial" of the testing technology depended on an interpretation of PKU in racial terms. The institutional and political priorities were bundled into the testing technology, foreclosing some questions while apparently answering others. As a white disease, PKU drew on readily applicable social categories ("white" and "nonwhite"), widely recognized and extremely important to the organization of health care and public health in the United States.

III. REDEMPTION

By September 1964, the Children's Bureau was urging the use of the Guthrie blood test on a routine basis for all infants. The inhibition assay method now made it practical, said a Bureau press release, "to carry out routine screening of newborn infants in hospitals for detection of this inborn error of metabolism." In the field trials, blood was extracted from more than 400,000 newborns at 505 hospitals. Thirty-nine cases of disease—visible in the blood—had been detected out of only 275 "presumptive positives" subjected to further testing. The frequency of PKU in this specially screened population, thus, was 1 in 10,347—higher than predicted when the trials began.

As the Guthrie test was rapidly embedded in state law,

43. Press Release from the U.S. Children's Bureau, PKU Blood Screening in Hospitals (Sept. 30, 1964) (on file with the U.S. Children's Bureau, National Archives and Records Administration, College Park, Md.).
44. See id.
45. See CHILDREN'S BUREAU, PUB. NO. 419, supra note 1, at 10.
legislation was justified in public discussions by a narrative of redemption: a claim that mandatory political control of PKU, mediated by the blood taken from new citizens, was a benevolent state intervention that saved PKU children from their own metabolism. With a proper system to manage blood, the state could redeem the vulnerable body by providing information. In turn, the blood of newborns could redeem both society and the individual marked with a metabolic disorder.

The redemption narrative was the one detail that was consistently included in materials given to new mothers and consistently invoked by legislators. It was the only biological fact in these contexts that mattered. Mothers were not told that PKU was a disorder of phenylalanine metabolism, that it was inherited as an autosomal recessive, or that it could be detected by an inhibition assay in which excess phenylalanine permitted bacterial growth. But they were told that it could be treated with a "special diet."

A Minnesota brochure, for example, emphasized that PKU damage could be prevented through a "special diet," while another brochure said that advocates for mentally retarded children "know that the best way of doing something about mental retardation is to prevent it from happening."46 A pamphlet used in Findlay, Ohio, included lurid title lettering asking new mothers, "How will your child's mind develop?" The text itself emphasized the efficacy of the controlled diet.47 And a Massachusetts leaflet given to parents presented the redemption narrative in classic form, telling parents that research has shown that "this mental retardation may be prevented if a special modified milk diet is started during the first few weeks of life . . . . [I]t is very important to find it early so that the special diet can be started before it is too late to be effective."48

The omission of details about the disease reflected the fact that redemption alone could justify the mass screening program. Mothers needed to know that salvation was possible, but they did not particularly need to know how the Guthrie test worked. In fact, other biological details were deemed irrelevant. The brochures they

46. Letter from Rudolph P. Hormuth, Specialist in Services for Mentally Retarded Children, U.S. Children's Bureau, to William Swatek, M.D. (Oct. 2, 1962) (copy of brochure from Fergus Falls, Minnesota, included with letter) (on file with the U.S. Children's Bureau, National Archives and Records Administration, College Park, Md.).
47. See id. (copy of pamphlet from Findlay, Ohio, included with letter).
48. CHILDREN'S BUREAU, PUB. NO. 419, supra note 1, at 66.
received presented the disease in ways that could and did explain and justify the removal of blood from their babies' heels. Meanwhile, just as the legislative mandates began to accumulate—with more and more states passing PKU legislation and accepting the idea of mandatory screening—the Children's Bureau began to have doubts about the enterprise it had sponsored and promoted.

IV. PUBLIC DOUBTS

Some significant problems emerged including ambiguous test results, problems with the maintenance of the diet, confusion about the disease itself, and doubts about the effect of diet on intelligence and psychosocial development. "A critical and objective review of the experience of the past fifteen years now indicates that the problem may not be as simple as was originally thought," wrote John A. Anderson and Kenneth F. Swaiman in a brief note introducing conference proceedings in 1966.49 The disease itself was a more diverse entity than originally believed, as reflected by the comment that "the spectrum of the basic and clinical aspects of the disease is wide."50

Some children whose blood contained high phenylalanine levels were being "confused with children who have classical phenylketonuria."51 In addition, some children who did seem to have "classical phenylketonuria" (whatever that might be) developed normally even without a restrictive diet. Anderson and Swaiman noted that "[t]he results of more thorough studies on family constellations suggest that the number of these mild or untreated cases may be a far greater segment of the clinical spectrum of the disease."52 Therefore, it was now absolutely critical, they urged, to "redefine not only the basic variations in the primary enzymatic defect, but also... to clarify the significance of the biochemical screening procedures now so widely employed."53

It had also become "essential to define more clearly the

49. See John A. Anderson & Kenneth F. Swaiman, Introduction to PHENYLKETONURIA AND ALLIED METABOLIC DISEASES (John A. Anderson & Kenneth F. Swaiman eds., 1967) (proceedings of the Conference on Phenylketonuria and Allied Metabolic Diseases which was held in Washington, D.C., on April 6-8, 1966).
50. Id.
51. Id.
52. Id.
53. Id.
diagnostic criteria for the disease."54 for it was now "common clinical knowledge" that variations occurred among PKU patients, for example, in fasting blood phenylalanine levels, the utilization of phenylalanine, and tolerance levels.55 Furthermore, the "sharp dichotomy" between carriers who did not manifest the disease and those with actual PKU was now "doubtful at the chemical level."56 The genetic dichotomy—heterozygote/homozygote—did not translate into a chemical dichotomy, and the chemical dichotomy did not translate neatly into a clinical dichotomy in patient outcomes. Some patients with "classical PKU" did not suffer from developmental deficits even without the diet. And some patients had high blood phenylalanine for a different chemical reason—"lack of transaminase activity"—and therefore did not have PKU but a "new condition."57

Moreover, "occult phenylketonurics" had been discovered in the British screening program—patients who had PKU but whose excretion of phenylpyruvic acid in urine was too low to give a positive reaction in the Phenistix test (the urine test used in the British screening program).58 Additionally, at least one set of apparently identical twins, both testing positive for PKU, had been studied in which one twin was of normal intelligence and the other severely retarded. L.I. Woolf, a physician presenting at the 1966 conference, concluded that "[t]he difference in clinical manifestations cannot be genetic in origin if [these twins] are monozygotic."59

It was also becoming clear that the blood test was picking up genetically "healthy" infants who did not "have" the genetic disease PKU but nonetheless were born with symptoms of PKU, including high phenylalanine blood levels and mental retardation because of maternal PKU. A December 1963 issue of the New England Journal of Medicine described three women whose high blood phenylalanine levels apparently produced mental retardation in all fourteen children born to them. These children did not have genetic PKU, but their bodily condition mimicked PKU—it was produced by the same biochemical processes and detected by the same tests. What disease

54. Id.
56. Id.
57. See id. at 33.
58. See L.I. Woolf, Large-Scale Screening for Metabolic Disease in the Newborn in Great Britain, in PHENYLKETONURIA AND ALLIED METABOLIC DISEASES, supra note 49, at 50, 51.
59. Id. at 58.
exactly did these babies suffer from? And who was being tested when the newborn's blood was taken? Guthrie noted that "[t]his is the first published evidence that phenylketonuria in the mother may be a significant cause of mental retardation in the offspring, due to the damaging effect to the foetus before birth caused by the mother's high phenylalanine blood level." 60

PKU, the disease itself, as an intellectual and clinical category, was being called into question as a consequence of the details produced by a widespread system of disease management. What exactly was PKU? How could it be identified? Perhaps the screening program was defining the bodily condition inappropriately, perhaps even in ways that could damage children.61 Anderson and Swaiman advised: "In the face of conflicting evidence it is now imperative that all aspects of the problem be reviewed." 62

The ensuing conference included papers on primary metabolic questions, dietary management, and the "role of government and legislation in [the] management of problems in medicine." 63 PKU was defined in these different contexts as an enzymatic defect with some impact on the central nervous system, a public health problem, a consequence of patient refusal of an unpalatable diet, a psychological problem, and a test of screening technologies and methods that could guide future screening programs for other diseases.

Toward the close of the conference, Howard University political scientist Joseph D. Cooper voiced some general criticisms of the PKU program, suggesting that the screening so rapidly adopted by so many states constituted an inappropriate use of state power based on inadequate scientific evidence. Cooper commented, "Mandatory legislation has been chosen as the medium for achieving program acceptance without regard to sensitive questions which concern the future practice of medicine." 64 But Guthrie quickly challenged Cooper's right to criticize scientists, remarking, "I don't think it is possible for you as a political scientist to discuss the scientific

60. Memorandum from Robert Guthrie, University of Buffalo Medical School, to Maternal and child health directors and laboratory directors participating in the trial of the inhibition assay for early detection of phenylketonuria, Detection of Maternal Phenylketonuria (Jan. 8, 1964), reprinted in CHILDREN'S BUREAU, PUB. NO. 419, supra note 1, at 60-61.
61. See Anderson & Swaiman, supra note 49.
62. Id.
63. Id. (table of contents).
evidence...”

In contrast, Guthrie presented himself as a deeply interested and invested scientist who developed and promoted the blood test “as a parent of a retarded child, and as the uncle of a phenylketonuric child. My niece, who is now eight years old, gave me impetus to develop the screening test.”

Cooper’s disciplinary distance, Guthrie suggested, prohibited him from speaking to scientific questions, while Guthrie’s own bodily, emotional, and personal investment in PKU (his familial experience) was central to his legitimacy as a spokesman for PKU screening.

Guthrie then defended mandatory screening by pointing out that “the laws compel the collection of a specimen. The details concerning the specimen are left up to the State health department...” Thus, the blood itself was the focus of the legislation. The state legislature could demand that the blood be removed from the body—it could pass laws that would “compel the collection of a specimen”—but its post-embodied fate depended on a different realm of expertise, that to be found in state health departments and scientific laboratories. Guthrie’s defense of the PKU screening program postulated that the blood of newborns was the material that could move across and link the political and the scientific.

**CONCLUSION**

In 1970, after PKU screening programs were virtually universal in the United States and in many European nations, the American Society of Human Genetics’ Committee for Social and Public Issues in Human Genetics began a study of “problems of large-scale screening for genetic metabolic disorders.” A “full scale evaluation of existing practices of the phenylketonuria program” was needed, with attention to “medical, scientific, logistic, administrative and economic aspects.”

65. *Id.* at 174.
66. *Id.*
67. *Id.* at 175.
68. Letter from Arno Motulsky, Chair of the Committee for Social and Public Issues in Human Genetics, American Society of Human Genetics, to Philip Handler, President of the National Academy of Sciences (Mar. 6, 1970) (on file with the Archives of the National Academy of Sciences, Washington, D.C.). The distinguished members of the committee included three luminous figures in postwar genetics: James V. Neel at the University of Michigan, James F. Crow at the University of Wisconsin, and Joshua Lederberg at Stanford University. Other members included Alexander Bearn of the Cornell Medical Center, Barton Childs of the Department of Pediatrics at Johns Hopkins University, and Robert F. Murray at the Howard University College of Medicine.
69. *Id.*
The final report, published in 1975, was an effort to come to terms with the emerging consequences of state-mandated blood testing and newborn screening. The committee was interested in the possibility of "storing biological specimens for later testing," and the blood taken from infants was constructed as a permanent public resource that could be archived for some unknown future use, including future testing as new diagnostic techniques developed. The Study of Inborn Errors of Metabolism—SIEM as it came to be identified—concluded that genetic disease had become a public health problem of national significance.

The blood extracted from almost every newborn in the United States for the last thirty-two years is a physical monument of the rise of genetic disease to medical prominence. Stored indefinitely in state laboratories, the babies' blood is an archive in which a particular construction of the body is preserved. The blood itself is a record not only in the sense that it records data about individuals, but also in the sense that its systematic management makes manifest some central properties of the biomedical and political construction of the body: fragmented for the purposes of obtaining information, the body moves into an information retrieval system and becomes a form of transportable data.

As a subject of state-mandated testing programs, the blood saves the public money, but the state's financial interests in the able body are not the only justifications for PKU testing programs. The blood is also a sign of faith that through testing redemption can be achieved—the sick can be healed, the mind restored. The child with PKU can be prevented from experiencing the degraded state of mental retardation as a consequence of the blood itself, which makes state intervention possible by providing the information needed to justify action.

As problems emerged with the twin technological parameters that shaped PKU—testing and diet—issues that seemed to have been resolved unraveled. The diet was neither as simple nor as effective as

70. See id. Motulsky said the group's goal was to "identify public issues in genetics and in various ways to foster discussion and public understanding in these areas." Id. He seemed to suggest that the purpose of studying PKU screening was to guide "future action in this field." Id. But he closed his letter of appeal to Handler by saying that the "screening problem" (not further elaborated) "is only one of many public issues in human genetics which need broad and more intensive attention." Id. The PKU study could produce, he hoped, "solid recommendations for action" and this "first venture" might provide "a mode of approach" that could be applied to other issues. Id.

71. Id.

72. See COMMITTEE FOR THE STUDY OF INBORN ERRORS OF METABOLISM, supra note 5.
early reports had suggested, and the test neither as reliable nor as unequivocal. Yet the institutions grounded in these technologies persisted and became the framework for other genetic tests. "Certainty" about both test and therapy disappeared, but the legislative frame built from that certainty persisted unaffected and could be adapted to other uses.

Presently, newborns in North America, Europe, Australia, and Japan are routinely screened for about a dozen metabolic disorders, not all of them treatable. The network of blood-spotted filter paper that this screening produces around the world has become a resource for researchers in academe and private industry, in a process one ethicist has called the "highjacking of legitimate newborn screening by researchers looking for easy specimens from the captive population of newborns." A physician at a French diagnostic center noted in 1993 that "for over twenty years, examinations were carried out on blood samples that were destined for entirely different uses," but that these "alternative" uses of blood were now coming under increasing scrutiny. He asked: "Do we have the right to conserve the blood, serum or DNA of an individual without their knowing what will be done with it?"

Other selected populations are screened for different reasons—perhaps because they are at a high risk for a particular disease (Tay-Sachs) or because they are in an age group in which chromosomal defects are likely. While such screening poses similar questions of privacy and consent, it does not involve the blanket screening of every newborn or the violation of a body (one critic has called it "technically an assault") that cannot provide informed consent. Neonatal screening is a particularly powerful and revealing network of political and biological control, and PKU remains its flagship disease.

A poorly understood and defined disease entity with highly variable expression and a difficult treatment therapy became in the

73. Bartha Maria Knoppers, Newborn Screening and Informed Consent, in NEW HORIZONS IN NEONATAL SCREENING 15, 19 (Jean-Pierre Farriaux & Jean-Louis Dhondt eds., 1994) (proceedings of the Ninth International Neonatal Screening Symposium and the Second Meeting of the International Society for Neonatal Screening which were held in Lille, France, on September 13-17, 1993).

74. Jean-François Mattei, Ethical and Legal Issues Associated with the Conservation of Blood Samples, in NEW HORIZONS IN NEONATAL SCREENING, supra note 73, at 41, 41.

75. Id.

76. Knoppers, supra note 73, at 18.
1960s and 1970s a political symbol of the potential power of applied human genetics. A genetic disease with plasticity, amenable to environmental control, presented the prospect of effective intervention with such force that it became unethical to question the test or the intervention, and certainly unethical to withhold them, even if many questions remained. Through an institutional, technological and social network, some uncertainties and questions about PKU disappeared because they ceased to be asked or to be open to being asked. Other uncertainties emerged as difficulties with the performance of the Guthrie test and the management of the low-phenylalanine diet became clear. The disease—PKU—came to conform to the available technologies and to the legislative mandates that defined its relevant properties.

How, then, was PKU made? It was made by technologies that foreclosed options—the Guthrie test; by state laws that mandated a particular clinical interaction; and by a redemption narrative that drove such legislation and that justified faith in both science and political control. The meaning of the fact that any particular body was unable to catalyze phenylalanine to tyrosine depended on a system of laboratory technology and legislative support. There was in this case no sharp line between the bodily experience of disease, the blood with high levels of phenylalanine, and the public health and laboratory systems that managed and made sense of both body and blood. It is not possible to extract PKU from the technologies that reveal it—the technician who autoclaves a Guthrie card is participating in making PKU, as are the laws that mandate tests for its presence and the manufacturers who produce the dietary supplement Lofenalac for PKU patients.

As the PKU case suggests, biological materials drawn from human beings, whether living or dead, are political commodities. The babies’ blood collected for PKU testing was treated in the ways many bodily materials in twentieth century biomedicine are routinely treated. The systems I explore are present in everyday biomedical testing of bodily fluids in a standard physical; in the institutional testing of inmates, employees, students, or military recruits; in epidemiological and biomedical research; and in the corporate, proprietary management of cell lines, tissue samples, DNA probes, and other fragments.77 Acquiring such materials generally involves

77. For an insightful exploration of these kinds of testing, see DOROTHY NELKIN &
political and social negotiation. This is obvious to those interested in obtaining DNA from isolated populations needed for the Human Genome Diversity Project, malformed stillbirths from mothers at Chernobyl, spinal fluid from African-American men at Tuskegee, blood from newborns to be tested for AIDS, or the brains of serial killers to be assessed for pathologies. Such materials contain reliable knowledge only when they have been shepherded through a process of extraction, testing, and preservation.

More generally, I seek to understand through what processes genetic disease acquired the properties it possesses today—as both proximate and ultimate cause of all disease and as a public health problem on a grand scale. The PKU case helps to make visible the piecemeal nature of this transformation. It is of particular interest as the data produced by the Human Genome Project continues to expand the range of genetic testing. The steady stream of new disease genes can quickly be accessed as textual signs of risk and future pathology. The ability to test asymptomatic children for late-onset disease has been the focus of particularly intense concern among ethicists and health professionals. As the PKU case suggests, technologies close options as well as open them, and can and do prevent inquiry as surely as they encourage it. As we embrace genetic testing and a model of all diseases as genetic—as genetic disease emerges as the central public health problem of the twenty-first century—it is perhaps useful to pause and consider how we make decisions about the presence or absence of genetic disease, and how genetic disease has conformed to available networks of technology and social management.

