Genetic Screening: States May Be Writing the Wrong Kind of Laws

During the 1960's, a majority of states in this country enacted legislation requiring that newborn babies be screened for phenylketonuria (PKU), a metabolic disorder that can cause mental retardation unless treatment is begun during the first weeks of life. As a result, an estimated 90 percent of babies born in the United States are screened for PKU before they leave the hospital. In most cases, their parents cannot object. Most frequently, they do not even know.

The authority of a state to mandate genetic screening is derived from its well-established power to protect the public health, as it does by requiring children to be vaccinated, for example. But when legislators extended that authority to include screening for inherited disorders, they moved into new and uncertain territory. After more than a decade of experience with PKU screening laws in more than 40 states, it is still not apparent that it is sound policy to govern genetic screening by statute. Nevertheless, that is what is happening. Today, questions about the proper role of the state in genetic screening are taking on new currency as states move from mandatory screening for PKU to mandatory screening for a number of other genetic diseases, some of which may not be diseases at all.

To get an idea of just how many states are initiating, or contemplating, expanded genetic screening programs, Philip Reilly, a legal scholar at the University of Texas Graduate School of Biomedical Sciences in Houston, recently surveyed all 50 states and the District of Columbia. At the present time, 14 states have programs for screening newborns for diseases other than PKU. At least 12 other states have an interest in broadening their programs.

What many states are doing is simply amending PKU laws by adding a string of new diseases as the technology for detecting them is perfected. Critics say this is no way to do business, that states are behaving the way Congress behaved a few years ago when it created a sickle cell anemia program, then a Cooley's anemia program (*Science*, 10 November 1972), then one for hemophilia, and so on—the "disease of the month club" approach. The diseases that states have been singling out for screening programs are rare, and many are not suitable for mass screening programs, although it is certainly worthwhile to study them on a research basis.

Problems arise because some of the diseases states screen for are, at best, poorly understood. In some cases, the value of the biochemical information one gets by screening is dubious; in others, there is no good treatment. There is great possibility for misdiagnosis. And, like it or not, there is always the problem of making people feel stigmatized by telling them there is something wrong with their genes.

What scientists would like to see in both federal and state law is a comprehensive approach to genetic diseases that recognizes that, although the symptoms and severity of diseases vary, they have much in common as far as the need for careful, accurate diagnosis and good genetic counseling and education of both physicians and the public is concerned. Two years ago, a group of geneticists went to Senator Jacob Javits (R–N.Y.) to ask him to drop a Tay-Sachs bill that had been urged on him by his Jewish constituents and to push instead for an omnibus genetics bill. Javits was responsive, as were members of the House. In late February, members of both houses met in conference to negotiate details of the comprehensive National Genetics Disease Act that is expected to become law very soon. It will create a special genetics disease unit in the Department of Health, Education, and Welfare and provide for programs in research, training of health professionals, and education. However, it does not mean that the federal government is going to start legislating mandatory screening for certain diseases. That remains in the hands of the states and whether they will decide to abandon taking a legislative approach to genetic disease is uncertain. However, some states, notably Maryland, are taking that direction.

The first simple, inexpensive, and therefore broadly applicable, test for PKU was developed in 1961. The logic behind using it on every baby was compelling. By analyzing just a couple drops of blood pricked from the baby's heel, one could tell whether or not excessive concentrations of the amino acid phenylalanine were present. Although some phenylalanine is essential for normal development, the excess amounts that accumulate in PKU babies, who are deficient in the enzyme needed to metabolize it, cause central nervous system and brain damage resulting in retardation. Putting PKU children on a low phenylalanine diet, which is to say a protein-free diet, until they are between 4 and 6 years old saves them from retardation. No legislator in his right mind could vote against a bill in favor of mentally healthy children. It was humane and economical as well, inasmuch as it is cheaper to screen for and save PKU babies than it is to spend thousands of dollars providing them institutional or other special care. Suddenly the arcane science of genetics made sense in the marketplace. By 1966, 43 states had PKU laws.

While legislators were busy with PKU scientists were busy learning how to detect a wide variety of metabolic disorders as they developed simple biochemical tests that would measure the concentrations of a particular amino acid or enzyme in blood or urine. Easy identification of certain chromosomal aberrations also became possible during the past decade, as did the ability to screen for sickle cell anemia. The easy ability to test made the situation seem deceptively simple. Doctors could identify too much or too little of a given enzyme, for instance, but could not always do anything about it. Then, in some cases, the association between a certain chemical and disease is only tentative. Furthermore, in thinking about mass screening for many genetic diseases, one must take into account the fact that each is rarer than the next. And so, critics of new state laws that specify screening for a half-dozen or more conditions that are only partly understood are beginning to ask a question that is becoming familiar in many areas of science: Should we, as a society, do something just because we have the technological capability to do so? Different states have different answers.

In 1973, Maryland said no and turned responsibility for genetic disease programs over to a new commission on hereditary disorders whose job is to decide when to screen and when to refrain. In 1974, New York said yes and amended its PKU law to mandate screening for a string of genetic disorders. Wisconsin is asking itself the question right now as it considers a new genetic screening bill which began last year as an "if you can screen for it, do it" piece of legislation that enumerated 16 separate conditions and is presently being redrafted into a more conservative proposal.

For the past 2 years, all infants born in New York State have been screened for PKU, sickle cell anemia, maple syrup urine disease, galactosemia, homocystinuria, adenosine deaminase deficiency, and histidinemia. At a total cost to the state of only $250,000 a year, it sounds like a bargain, but not everyone thinks it is.

Early last year, Representative Edward I. Koch (D–N.Y.) introduced a bill in the House that would extend the provisions of the New York law nationwide. A couple of months later, Senator Hubert H. Humphrey (D–Minn.) introduced similar legislation in the Senate, and a press release described the bill as one that would require federally assisted hospitals to "routinely test newborn infants for metabolic disorders that could retard brain development." Neither the Koch bill nor the Humphrey bill has been acted on, and may not be now that the National Genetic Disease Act is so close to passage.

Scientists and legal-scholars fault the disease-by-disease approach to mass screening, well-intentioned though it may be, on a number of grounds. Sickle cell screening points up two of them. In the first place, critics say there is no point in identifying sickle cell babies at birth because there is no treatment that can be offered them then and the clinical signs of the disease will not show up until later. Second, for technical reasons, it is not possible to identify sickle cell babies without also identifying those that carry the sickle cell trait, a benign condition that presents problems only if two trait carriers plan to bear children. Many individuals think the trait is a stigma, although it is utterly groundless to think so. Many geneticists oppose newborn sickle cell screening because it may do more harm than good.

Then, there is the matter of mental retardation. Sickle cell anemia does not cause mental retardation. Neither, for that matter, does adenosine deaminase deficiency, another of the conditions singled out for screening in the New York law. Yet it is certainly possible that they may be linked together in the public mind as a matter of guilt by association.

There are other questions. Adenosine deaminase deficiency, which was, for instance, mentioned originally in the pending Wisconsin bill, is a condition that has been associated with a rare and lethal immune disorder, combined immunodeficiency disease (CID). In the absence of adequate adenosine deaminase, the lymphocytes of the immune system cannot develop properly and the patient is left without natural immune defenses. Symptoms of CID show up by the time a child is 4 to 6 months old. The only available treatment is bone marrow transplantation. Some immunologists believe that the only advantage of neonatal screening in this case is that, if one found an affected child, one would have a 4 to 6 months head start in looking for a genetically compatible bone marrow donor if the child had no sister or brother whose genetic makeup matched his own. It may be only a modest advantage—CID children

Rocky Speaks at AAAS Meeting

Boston. Vice President Nelson A. Rockefeller topped off the AAAS meeting on 23 February with an address which mixed encomiums for American science with warnings of "a certain questioning of" American technological achievements and a "growing cynicism respecting their value." Rockefeller clearly had mainly in mind the current debate over development of nuclear power, declaring "nuclear power is not going to go away . . . nor can it be suppressed by any group or nation."

Rockefeller had pointed criticism for opponents of nuclear power, who were represented in earlier, well-attended energy sessions of the meeting. "There is always risk in invention, in discovery . . . and yet listening to the debates and reading the emotional arguments about energy sources and energy technology, one wonders at times whether we are dealing with a world of science and fact or a world of superstition and fear." Rockefeller went on to say better mechanisms must be developed for "bringing into focus the facts and informed, mature, objective judgments of the scientific community."

The AAAS annual meeting continues to be the nation's biggest intellectual bazaar, but this year there was little tumult and hardly any shouting. The spirit of 1976 (the meeting theme was Science and Our Expectations—Bicentennial and Beyond) seemed to be a reflective one. AAAS top officers noted that in recent years science had been blamed for environmental damage and for use in the Vietnam war. Now, however, retiring AAAS president Margaret Mead observed, people are realizing that the "misapplication of technology" was culpable. Resentment against science among students and the public generally is easing, and the government attitude toward basic science is more favorable.

The disruptions of previous years were absent from this year's sessions. Political activists and AAAS officials seemed to have traded confrontation for coexistence, if not congeniality. The Science for the People group, which had been the chief antagonist of the AAAS in past years, had a room of its own and even planned several sessions for the regular program.

Meeting attendance stood at about 4700 on the next to the last day of the meeting (23 February), somewhat less than AAAS planners had hoped for. They saw the explanation for the shortfall in the scheduling of the meeting while many colleges and universities are in session and in the tightness of travel funds in the current economy. The weather, often a factor in snarling transportation schedules during AAAS winter meetings, was generally favorable, but the ubiquitous flu bug took its toll of participants, staff, and audience and the hacking cough was the characteristic sound in the halls.

Perhaps the most notable innovation at this year's meeting was the special effort made to invite and accommodate handicapped persons studying or working in science. AAAS staff and volunteers provided assistance and services to the record number of handicapped—between 150 and 200—who attended. These services ranged from special transportation arrangements and a resource room for the handicapped to interpreters for the deaf at meetings, escorts, and such small but helpful touches as a short version of the program in Braille and emergency repair facilities for wheelchairs and other devices.

The AAAS Council, the big elective body which meets annually to act on major policy matters, concentrated this year on international issues in voting resolutions. Two of three resolutions approved dealt with United States–Soviet relations and the third with the United Nations General Assembly. In the latter resolution, the council endorsed a AAAS board resolve opposing the assembly position in declaring Zionism a form of racism.

In a council resolution prompted by the Vladivostok agreement on nuclear arms, the council noted that agreement had resulted in a "destabilizing" increase in weapons levels and urged the U.S. to work for agreements on several points and "Move toward a phased mutual reduction of nuclear weapons levels that will ultimately lead to a renunciation of their use in warfare."

The final resolution cited the "violation of internationally recognized scientific norms" in the Soviet Union and asked the AAAS president to express concern to the president of the Soviet Academy of Science that Soviet practices be changed to permit emigration of scientists who seek it and "to grant human rights intrinsic to the advancement of world science."—J.W.

have had successful transplants at 1 to 1½ years of age. Furthermore, CID is a rare disease; probably not more than 25 cases are diagnosed in the United States in a year. Should we, as a matter of legislative policy, expend resources in a situation such as this? The point is not so much whether there is any reason not to screen as whether there is any reason to do so.

Lawyer Philip Reilly thinks it bad policy to mandate screening for diseases such as CID. It is, he notes, "hardly a major public health problem." Reilly fears what he sees as a trend toward screening that will "label people with diseases that aren't" and have states spending money to look for diseases they may never find. As an example, he cites the small state of Rhode Island, which screens for maple syrup urine disease, a disorder that leads to mental retardation but has an incidence of only 1 in 300,000 births. "In Rhode Island, they may pick up someone once in a decade," he says. If states are going to screen, Reilly would rather have them screen for more common, treatable disorders.

"Why," he asks, "don't we screen for neonatal hyperthyroidism which causes mental retardation and can be treated?" During the past couple of years, investigators have developed a test for this disease which occurs in 1 out of every 6000 births (or 500 infants a year), making it more common than PKU. In any case, he thinks the screening should not be a matter of law.

Even PKU screening, well established as it is, is not without its problems which, are underscored by geneticist Neil Holtzman of the Johns Hopkins University School of Medicine in Baltimore. In a recent article in the *New England Journal of Medicine* (16 October 1975), Holtzman and his colleagues report on a child who had been diagnosed at birth as having PKU and was placed on a low phenylalanine diet. Blood checks indicated that his phenylalanine levels were under control; nevertheless, by the time he was 7 months old it was evident that he was retarded. Further careful biochemical studies revealed that the child did not have classic PKU at all but a related disease involving a deficiency of an enzyme known as dihydropteridine reductase. This case illustrates the kinds of problems that can arise when complex metabolic disorders are handled in an oversimplified way. The need for sophisticated follow-up of babies picked up in an initial screen is great but may not always be provided.

At this point, it is not possible to say that the child would have been spared retardation had he been correctly diagnosed from the start—there is no clear therapy for his deficiency—but it is certain that he need not have been placed on a low phenylalanine diet. The diet involves more than abstinence from just a few types of foods. It involves abstinence from virtually everything except a special substance called Lofenalac that comes as a powder and can be mixed with water to be fed either as a liquid or a mushy pablum. It costs about $60 a month. Although Lofenalac is of inestimable value to the PKU child, who must live on it until he is between 4 and 6 years old, it is not an easy thing for families to contend with, especially when the child becomes old enough to snitch other foods. If a child is misdiagnosed as having classic PKU, and is restricted to Lofenalac for very long, it can be downright harmful. Although increased blood concentrations of phenylalanine can mean PKU, they do not do so in every case. Far from it. Many individuals have mild increases that appear to be benign. A low phenylalanine diet would deprive them of an essential amino acid and could cause the very retardation it is meant to prevent. Holtzman observes that with current screening, of approximately 3 million babies born each year, 3000 will have positive test results. Of those, only 200 will have classic PKU.

The same complexities surround the diagnosis of galactosemia and homocystinuria, each of which is referred to as if it were a single disease although each actually occurs in different forms. One form of galactosemia, for example, causes mental retardation and can be treated by keeping the patient away from milk products which he cannot metabolize properly. Another form is benign and need not be treated at all. Researchers are concerned that, as states move into mass screening for conditions such as these, the individuals doing the screening be sophisticated enough to know the difference.

Unfortunately, many state laws were written without regard to quality control of testing or to other important considerations such as provisions for follow-up therapy or genetic counseling. A familiar problem with medical legislation is that it is drafted by eager legislators without benefit of sound scientific advice. Wisconsin is a case in point. A year ago, state Representative Joseph Czerwinski introduced a disease-by-disease bill somewhat like the New York statute. According to Czerwinski's aides, it took the scientific community a while to realize that the bill even had been introduced and, when it did, its response did not endear it to the politicians. Said one aide, "We've had a lot of griping about the bill but it has all been negative input and we can't do anything with it." Eventually, however, scientists and lawmakers got together and, at a meeting a couple of weeks ago, sat down to draft a bill that takes a more comprehensive approach.

The ideal situation may be one in which scientists and lawmakers work together from the start, and some states are moving in this direction. The Wisconsin bill will establish an advisory body composed of a variety of individuals, including scientists, to make suggestions about any future legislation. The Massachusetts legislature not long ago created a commission of scientists and others to advise it on bills that would affect research and medical care (*Science*, 28 March 1975). But it is Maryland that has gone the farthest. Although not everyone agrees with every provision of Maryland's law, it is nonetheless regarded as a leader in providing sensible and flexible handling of screening issues. With a few modifications, the Maryland statute has been adopted as a model law by the Council of State Governments.

Maryland Takes Lead

In the spring of 1973, the Maryland legislature created an 11-member Commission on Hereditary Disorders and gave it authority to write the rules and regulations governing all genetic disease programs in the state. In doing that, the legislature implicitly said that such programs should not be created, one by one, by statutory law, but should be handled by some more flexible administrative body. The commission, designed in part to be a forum for the discussion of the ethical questions that are pertinent to genetic disease programs as well as the technical problems, is comprised of two state legislators, four scientists, and five laymen. Its monthly meetings are completely open to the public.

The origins of the Maryland commission date back to 1972 when the state passed a sickle cell anemia bill that had been introduced by Senator Julian L. Lapides (D–2d Baltimore). Holtzman, from Johns Hopkins, and other physicians became concerned that the state, which already had a PKU bill, was following a course that would lead to the passage of one genetic disease bill after another, piecemeal. Although they found the Lapides bill itself to be essentially sound, they disliked the precedent inherent in it. So, in October 1972, they went to Lapides. "I remember Tony [Holtzman] coming to ask why the General Assembly had passed a bill about a single genetic disorder when it ought to be writing a single, flexible law to take care of genetic disorders generally. He was asking me to call for the repeal of my own bill, which I'd worked pretty hard on. Still, I had no interest in backing a bad law, and the idea of a broader bill made sense." During the following 3½ months, Holtzman and his associates met frequently with one of Lapides' aides. By mid-

January, they had a bill ready to go. Lapides' sickle cell bill was repeated.

In comparison to other states' genetic disease laws, which tend to say that screening for PKU or whatever shall be done and leave it at that, the Maryland statute establishing the commission is a lengthy and philosophical document. While granting the commission unusual authority to actually write regulations on the one hand, it carefully lays out the principles that must govern its actions on the other. Thus, no programs can be adopted unless the public—particularly those groups that will be most directly affected—has been consulted. The principles also provide for the confidentiality of medical information, counseling services for persons screened, and the right of any person to refuse screening for any reason. Furthermore, the principles preclude any restrictions on childbearing.

Says Lapides, "We realized that research and various programs on hereditary disorders raise extremely important questions about how medical science will become involved in couples' decisions to conceive and bear children. In the short run, we are confident that a well-run program on certain hereditary diseases, conducted by ethical and competent professionals, should alleviate a great deal of human suffering. But we just don't know where this will lead in the future. One thing was clear in writing this bill. These decisions must not be made in medical laboratories. They have to be made in public. That's why we made the commission an open, public forum."

Experience with the commission so far indicates that it is working. At present, for example, it is preparing regulations for a sickle cell program, and at a recent meeting it devoted time to discussing in detail the various tests that are available to detect hemoglobin abnormalities. This is precisely what scientists throughout the country would like to see happen. The legislature cannot weigh the accuracy of method A versus method B, nor can it know which method is suitable for mass screening and which needs more research. The commission can do this, and it can easily change its rules as medical advances occur.

The commission is also busy with a new PKU program. Maryland and the District of Columbia are the only two governments that have repealed mandatory PKU screening laws, albeit for different reasons. In Maryland, the mandatory law was repealed because the commissioners fervently believe that all screening should be strictly voluntary. The District dropped mandatory screening for cost-benefit reasons. PKU is extremely rare among blacks, who constitute a large majority of the District's population. According to Holtzman, in 3 years the District screened 77,000 babies at a cost of $135,000 and did not pick up a single case of PKU.

Although many persons experienced with genetic screening think the voluntary nature of Maryland's new PKU program is laudable, they also fear that the new program may cause problems because of a provision requiring informed consent that goes into effect 1 July 1976. When you start talking about truly informed consent, you are talking about educating people to an extent that can hardly be called a usual feature of present medical practice. Brochures explaining PKU and consent forms are being prepared and physicians are being asked to start informing their patients, but no one is sure how it will work or whether the provision will discourage parents from participating. Holtzman tried to get a $10,000 grant so that informed consent procedures could be tried in a few hospitals before they go into effect statewide in July, but he had no luck.

However, the commission is getting a bit of anecdotal information on informed consent as a by-product of another aspect of its PKU program. Although testing newborns for blood phenylalanine concentrations is prudent, it is not sufficient to catch all PKU babies. Often, concentrations that appear normal within days of birth may rise after 8 days or more of life, well after the baby has been discharged from the hospital. Therefore, the commission has asked pediatricians to test for PKU when babies come in for their 1-month checkup. And, it is asking doctors at that stage to obtain only oral, not written, consent. Some are discovering, when they explain they want to take a second PKU test, that mothers do not remember being told that there had ever been a first.

At the present time, most of the social and ethical issues relating to genetic screening have to do with childbearing in one way or another. If a mother has one affected child, should she be allowed to conceive again and risk having another? If a mother knows, through in utero diagnosis, that she is carrying a defective baby, should she be forced to have an abortion? These questions are on the horizon. But there is another question, too, that will have to be faced soon because of advances in understanding the relationship of genetics to other sorts of diseases. Heart disease is a good example. Researchers today have preliminary evidence linking certain genetic constitutions with heart disease in adulthood. If, or more probably when, those links are more clearly known, society will have to confront the possibility that it will want to regulate the lives of potential heart victims; a kind of enforced preventive medicine, if you will. Maryland's broadly constituted, wholly open commission approach may prove to be an invaluable precedent in the handling of sensitive social issues that should not be left to scientists or lawmakers alone.

—BARBARA J. CULLITON

Oil Drilling in the Beaufort Sea: Leaving It to Luck and Technology

Plans to sell leases for potential oil- and gas-bearing tracts on the U.S. outercontinental shelf (OCS) continue to generate outcries from state and local officials and environmental leaders worried about possible adverse impacts. But even as this public furor has been going on in California, Alaska, and elsewhere, the Canadian government has been moving quietly toward a final decision to allow exploratory oil drilling to begin in that part of the Arctic Ocean known as the Beaufort Sea, an OCS province so fraught with environmental problems and hazards that the technology necessary for recovery of the oil and gas that might be found is still far from being available. A blowout of an exploratory well could lead to massive losses of fish, ocean mammals, and birds—including tens of thousands of migratory waterfowl—along some 400 miles of the Alaskan coast as well as along the Canadian coast.

In 1973 the Canadian government granted Dome Petroleum Ltd., a Canadian company based in Calgary, "approval in principle" to conduct exploratory drilling at two sites in the southeast Beaufort Sea. One of these sites is some 46 kilometers from land, at a water depth of 26 meters; the other is 83 kilometers offshore, at a