Newborn Screening- UC 260

Edward B. Goldman, J.D.
Health System Attorney
University of Michigan
November 13, 2003

Purpose

- We will review newborn screening (NBS) history
- Look at current NBS practices
- Discuss current technology for NBS and its effect on NBS
- Consider what ought to be NBS policy.

What isn't NBS?

- It is not genetic screening to determine if people should get married.
- It is not preimplantation testing.
- It is not fetal testing.
- It is not genetic testing for minors or adults to determine presence of a genetic condition (population screening for susceptibility to disease).

What is NBS?

- Removal of a small amount of blood from a new born (generally in the first 24 hours of life) and tests of that blood for several specific conditions that could cause "silent damage" (retardation up to death) if not immediately identified and managed (generally by dietary changes).

History

- Started in 1962 when Robert Guthrie and Robert MacCready in Mass. Tested every newborn for phenylketournia (PKU).
- PKU patients have a hereditary enzymatic defect so that their livers cannot break down phenylalanine into tyrosine.

History 2

- In 1951 a physician in England (Horst Bickel) developed a baby formula where phenylalanine was removed. He did this at the insistence of a mother with a 17 month old child diagnosed with PKU by Dr. Bickel.
- Robert Guthrie, a Professor at Buffalo, had a child with mental retardation.

History 3

- Dr. Guthrie was working on treatment and "cures" for mental retardation. In 1958 he developed a test for PKU that required only 3-5 drops of blood (up to that point any test required 15-20 cc's).
- The test was simple (drop of blood on filter paper with substance to inhibit bacteria which was reversed by presence of phenylalanine.

History 4

- 1961 Dr. Guthrie's wife's sister had a baby who had PKU but was not diagnosed until age 15 months at which point brain damage has occurred.
- He became convinced that universal NBS was required.
- He refined his test so that it could be done with one drop of blood from a heal stick.

History 5

- Dr. Guthrie began a national lecture campaign and a writing campaign about PKU and NBS.
- Children's Bureau in D.C. gave him a grant to test 400,000 infants. This showed large scale testing was possible.
- Dr. MacCready was trained by Dr. Guthrie and then returned to Buffalo and found 4 PKU cases in 9,000 patients.

History 6

- 1963 Mass. Became the first State to mandate NBS.
- In 1963 the journal Pediatrics published his results and parents began demanding testing.
- By 1966 a majority of States mandated testing and today all States do.

History 7

- Dr. Guthrie turned his attention to other disorders and developed tests for 30 different treatable conditions all of which could be diagnosed in a NBS program.
- He was offered a penny for every filter paper used for his test but he declined saying he wanted the test to be as inexpensive as possible. He never made any money from his discovery. He died in 1995.

Current NBS Practice

All States now test for certain conditions.
Michigan, for example, tests for:

Disorder	Incidence	Treatment
PKU	1:9,000	Diet
MSUD	1:232,000	Diet
Galactosemia	1:42,000	Diet
Biotinidase	1:34,000	Diet

Current Practice-Michigan

Condition	Incidence	Treatment
MCAD	1:20,000	No fasting
CH	1:2,000	Diet
CAH	1:20,000	Diet
Sickle Cell	1:600	Penicillin
Hearing	?	Hearing aid

Current Practice

- Some States test for 30 disorders while others test for 8 or less.
- Sen. Christopher Dodd D-Conn. had a baby in 2002. Conn. Tests for 30 disorders but Virginia tests for 8. Sen. Dodd wants a Federal law which could, he says, save 1,000 lives per year.

Current Practice

- In 2002 Jill Woods, a mother from Alexandria, Va. Lost her daughter 3 days after birth to a metabolic disorder called CPT-II. She wants mandatory national testing for all possible conditions.
- The March of Dimes is urging uniform NBS.

Current Practice

- There are over 1,300 known metabolic diseases. Screening is currently done for between 8-30.
- Screening is done by each State using State funding.
- What if you discover a baby who is a carrier but not itself effected?

Current Practice

- England and other European countries have stopped testing for Galactosemia since they believe intervention does not extend life. On the other hand the UK did not test until day 6-10 so it may have been too late.
- They also stopped MSUD and Biotinidase because “too rare”.

CF-an example 1

- CF (Cystic Fibrosis), an inherited disease, produces mucus that damages respiration and digestion. Life expectancy is approximately 30-40.
- 50% of all cases are diagnosed by 6 months and 90% by age 4.
- Would NBS be useful?

CF-an example 2

- A 1970's blood test allows CF to be diagnosed at birth.
- 1985-Researchers at U. Wisconsin screened every newborn in Wisconsin and assigned every CF positive baby to a treatment (parents told dx. and received dietary intervention) or a control (no info.) group.

CF-an example 3

- Was this an ethical experiment? Physicians say treatment was of unknown value and if not for the study there would have been no diagnosis anyway. i.e. Parents no worse off.
- 1991-Paper in Am. J. Clinical Nutrition reports early intervention results in normal growth for first 5 years.

CF-an example 4

- Study continued until 1994 when State of Wisconsin required CF NBS. Parents were never told results.
- Linda and Charles Andre had a daughter in 1993. She was positive for CF but parents were in control arm so were not told. Child was diagnosed in 1995 but by then the Andre's had another baby. Their Wrongful Birth suit is pending.

CF-an example 5

- It is still unclear if early intervention in CF patients will alter long term outcome.
- Question: What is the cost/benefit of NBS and is this even an appropriate question to ask?

The Effect of Technology

- Classic approach: One test for one condition. If State tests for 8 conditions there are 8 blood spots and 8 tests.
- New approach: Tandem Mass Spectroscopy (TMS). One blood spot with 30-50 results. Only current way to test for MCAD and other long chain deficiencies.

TMS

- Issue: many of the things TMS can identify have no intervention so do we want to know?
- "Your child has LCAD, a very rare genetic condition. We don't know exactly what it is, what it does or how to manage it but we thought you may want to know. Have a nice day".

New Technology

- On the other hand: TMS can identify certain conditions such as MCAD which causes the body to have problems breaking down fatty acids which can result in infant death.
- TMS was used to test blood samples from 7,058 infants whose death was called SIDS but actually were MCAD.

What Ought Policy to Be?

- Wilson-Junger Criteria
- 1. Condition should be an important health problem
- 2. Should be accepted treatment
- 3. Need facility for treatment
- 4. Latent (or very early) stage
- 5. Test is acceptable to the public

What Ought Policy Be? 2

- Wilson-Junger Criteria
- 7. Must understand the disease
- 8. Policy on whom to treat
- 9. Balance costs against medical care as a whole
- 10. Continuing case finding process.

Policy 3

- What conditions should we test for? CF in or out? Hearing in or out?
- Should there be a national panel of tests? If so who should pay for testing?
- Who should pay for follow-up and formula?
- Why limit to newborns?
- Is NBS cost beneficial? Best bang for the buck?
- Is parental consent necessary?

Does NBS Work?

- The CDC has been evaluating programs in every State (4 million screens each year).
- Georgia-8 conditions. 199,387 specimens. 135,163 satisfactory specimens. So repeat draws and tests required. 93 positive findings. No system for long term follow-up.

Current Status of NBS

- HHS and American College of Medical genetics are working on a recommendation for NBS for genetic diseases with a set of criteria for adding a test. The group will also recommend minimum State standards for programs and discuss long term care and follow-up.

Policy Discussion

- Need to consider the questions of:
- 1. What is possible?
- 2. What is useful ? (need to define "useful")
- 3. What is cost beneficial ?
- 4. Who ought to consent?
- 5. Who ought to pay?

Conclusion

- Life is always interesting but rarely simply.
- If you believe there is a simple solution to a problem you should either win a major award for elegant work or worry a lot.