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Is Universal Newborn Screening for Congenital CMV Good Public Policy?

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Disclosure Slide

I do support implementation of universal newborn screening for congenital cytomegalovirus infection

☑ Yes

☐ No

Case Vignette - 2025

A 35 year old G5P4 woman is admitted in labor. She has had an uneventful pregnancy and has no medical problems. She quickly progresses through labor and delivery and gives birth to an 8 pound, 10 ounce baby boy with APGARs of 9 at one and five minutes. The infant latches and breast-feeds vigorously and is alert and active in the nursery. He passes his NHS and is discharged at 48 hours of age. As he is discharged, the post-partum nurse obtains a mouth swab for his CMV PCR screen.

Followup…

The infant has normal well-baby visits at 2 and 4 months. His head circumference tracks along at the 75th percentile with normal interval growth parameters. At the four month visit he is social and interactive with a social smile and normal developmental milestones. As the visit finishes the pediatrician notices that his saliva PCR from the newborn nursery is positive for CMV.

What does she tell the baby's mother? Should she be mandated to instruct the baby's mother about CMV? What additional studies are warranted?

Annual Estimated Impact of Congenital CMV Infection and Disease in Europe and the United States (Dollard et al., 2007)

Category of Infants	Total
Total number of live births/yr	8,600,000
Average rate of congenital CMV infection (%)	0.7
Total number of newborns with CMV infection	60,200
Number with symptomatic infection (12.7%)	7,645
Number with fatal disease (~4%)	306
Number of survivors with sequelae (40-58%)	3058-4434
Number with asymptomatic infection (87.3%)	52,555
Number with sequelae (13.5%)	7,095
Total number with sequelae or death	**10,459-11,835**

American College of Medical Genetics Principles for Defining Criteria for Newborn Screening and Selection of Conditions for Newborn Screening

- ACMG review of 84 conditions including 3 infectious diseases
- Scoring system
  - Potential for treatment
  - Analytical characteristics of screening test
  - Availability of resources to diagnose, treat and provide care for screen-positive infants
- “There must be demonstrated benefit of early detection, timely intervention and efficacious treatment of the condition”

Watson et al., Pediatrics, 2006;117:S296

The Law…

THE SECTION ON

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

INFECTIOUS DISEASES

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NEWSLETTER

The Utah CMV screening law was criticized in the Spring 2014 Newsletter from the American Academy of Pediatrics Section on Infectious Diseases by William M. McDonnell, JD…

Beware Well-Intended Cytomegalovirus Legislation

William M. McDonnell, MD, JD
Chair, AAP Committee on Medical Liability and Risk Management

New Cytomegalovirus Law

There is an oft-cited aphorism that "the road to hell is paved with good intentions," which comes to mind after recent legislation regarding congenital cytomegalovirus syndrome. Traditionally, regulation of the practice of medicine in the United States has been left to members of the profession itself. In the dynamic field of medicine, clinicians, researchers, and other scientists are best-positioned to determine what medical practice standards are appropriate, and when those standards should change in light of evolving scientific knowledge. When clinicians fail to provide care consistent with these practice standards, medical malpractice liability may be imposed.

A recent law enacted by the Utah Legislature (H.B. 81, now codified at U.C.A. §26-10-10) took a different approach, and if duplicated in other states, may threaten physicians' abilities to practice medicine in a manner consistent with the best available science.

- The pediatrician is required to inform the parents about congenital CMV, and discuss "available methods of treatment".
- Subsequent educational materials developed by the Utah Department of Health specifically mention antiviral therapy in general, and treatment with valganciclovir in particular.
- After H.B. 81, any Utah pediatrician who fails to offer antiviral therapy to a child with CMV-related hearing loss will almost certainly face substantial liability risks, regardless of current or developing scientific evidence.
- Many Utah pediatricians have observed that they "resent being pushed into this off-label use of valganciclovir."

Ganciclovir – Economic Evidence of Benefit

- Initial study of six-week course of GCV did not include a placebo control group
- Not known if benefits of six-month course of therapy are sustainable
- All infants in the six-month protocol were symptomatic and none were identified by screening programs
- Economic cost-benefit analysis of CMV screening is largely dependent on assumption that GCV prevents need for cochlear implantation[1] – remains unproven

[1] Bergevin et al. Combatting Cytomegalovirus: A Cost Benefit Analysis of a Utah Department of Health Initiative Poster P1, this meeting


Help!!!
The Gov't Has
My DNA
it'smydna.org

The Rapidly Changing Landscape of Newborn Screening in Minnesota…

- Citizens' Council for Health Freedom (CCHF), St. Paul, Minnesota
- A 501(c)3 non-profit organization founded in 1998
- Intense lobbying effort contributed to events in Minnesota Senate session in 2011 which saw introduction of SFB1017 (SF760) by David Hann (R-Eden Prairie)
- Bill changes newborn screening to "opt-in" system
- Bill mandated destroying blood spots after assays completed and eliminated long-term storage
- Bill would put MDH labs out of compliance with CLIA laws and would have ended newborn screening registry

Bearder vs. State of Minnesota

- *Bearder v. State of Minnesota* was brought by nine families who wanted the state to obtain written informed consent to collect, store or use infants' blood samples
- The lawsuit was spearheaded by the Citizens' Council for Health Freedom
- The opinion centered on the meaning and interplay of two Minnesota laws: the newborn screening statutes, Minn. Stat 144.125 – 144.128 (2010), and the Minnesota statute entitled "Treatment of Genetic Information Held by Government Entities And Other Persons," Minn. Stat. 13.386 (2010; also known as the "Genetic Privacy Act"
- The Act prohibits the collection, use, storage or dissemination of a person's genetic information without written informed consent

Bearder vs. State of Minnesota

- The Minnesota Supreme Court Ruled:
  - (1) the blood samples collected and stored by the Department were genetic information subject to the restrictions of the Genetic Privacy Act; and
  - (2) the newborn screening statutes provided an express exception to the Genetic Privacy Act only to test the samples for disorders and to store the test results, and **NOT** to collect, use, store, or disseminate the blood samples for any other use without written consent.

NATURE | NEWS

Minnesota starts to destroy stored blood spots

Court ruling that the state must get consent to store samples from newborn screening could hinder biomedical research.

Meredith Wadman

03 February 2012

Minnesota's state health department has this week begun to destroy blood samples that are routinely collected to diagnose serious inherited and congenital diseases in newborn babies. It was compelled to do so by a state Supreme Court decision that such samples cannot not be stored or used for anything except diagnosis without the informed consent of the parents.

Heel-prick tests in Minnesota can be used to screen newborn babies for 53 serious diseases, but the samples are also crucial for biomedical research.

ISTOCKPHOTO

"We're going to begin destroying a valuable public health resource, the residual blood spots from about 200 babies born in Minnesota each day," said Edward Ehlinger, Minnesota's health commissioner, in a press release on 31 January. He warned that the new policy "will compromise our ability to assure the quality and accuracy of the newborn screening program". The Minnesota Department of Health (MDH) will now actively ask parents for consent to store blood spots collected from infants who have been diagnosed with one of the 53 diseases tested for, and automatically destroy samples from children who have been given the all-clear.

Minnesota Senate Bill SF2047

- April, 2014 the Newborn Screening Program Modifications bill (SF 2047) passed on a 41 to 22 vote and was signed into law by Governor Dayton
- The new bill enables MDH to retain these spots indefinitely again, and to use them and test results in research related to newborn screening
- Parents are able to choose if they do not want their child's samples and results stored
- The bill would require more education for parents about newborn screening, and would allow the samples and results to be used in public health studies not related to newborn testing if the parents or guardians provide their written consent
- If a parent chooses against storage, or has a change of mind and revokes consent they had given previously, the test results must be destroyed within one week of such a request

NATURE | NEWS

Minnesota to resume storing newborn blood samples

Law allows researchers to retain blood spots indefinitely, overriding a court ruling.

Sara Reardon

09 May 2014

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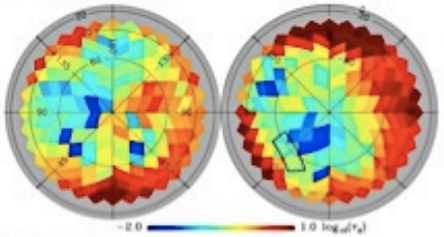
Minnesota will once again allow blood spots to be kept and used for further research following routine newborn screening of genetic and congenital diseases, thanks to a bill signed into law by the state's governor, Mark Dayton, this week. But privacy advocates opposing the law say that they will keep fighting to prevent newborns' DNA from being stored indefinitely.

The bill effectively reverses a 2011 ruling by the state's Supreme Court, which said that the practice violated the state's genetic-privacy laws. Under court orders, health officials destroyed more than 1 million blood spots dating back to 1997. The new law, which goes into effect on 1 August, will allow officials to keep the blood spots indefinitely.

Top Story



Full-galaxy dust map muddles search for gravitational waves

Planck probe's survey of polarized light casts further doubt on BICEP2 discovery claims and could complicate Planck's own plans.

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Reactions to SF2047

- The ACLU of Minnesota called the bill "**a dangerous effort to enable unlimited retention and minimize parental consent**," and noted "obtaining informed consent after newborn screening for all purposes is not only possible but practical."
- The Citizen's Council for Health Freedom in a statement reacting to the vote said the Senate "just **awarded state government ownership of the genetic information** of every newborn baby in Minnesota…it just voted to repeal genetic privacy rights at birth"
- The Council for Responsible Genetics' President Jeremy Gruber stated the bill was "…a strike against privacy rights", and that there is "**little transparency in how newborn samples are handled**".

http://www.genomeweb.com/clinical-genomics/minn-senate-passes-bill-restore-newborn-screening-bloodspot-data-retention-polic

TESTING UPDATE

NEWBORN BLOODSPOT RETENTION REINSTATED IN MINNESOTA

Practice expected to benefit larger newborn screening studies, public health, disease research

Minnesota's law prohibits the sale of bloodspots but allows sharing deidentified blood samples and test results for research conducted outside of the Minnesota Department of Health.

CCHF and the Minnesota Chapter of the American Civil Liberties Union questioned whether deidentified genetic information made available for medical research could be kept truly anonymous.

Newborn bloodspot retention reinstated in Minnesota
Am. J. Med. Genet., 2014, 164: viii–ix. doi: 10.1002/ajmg.a.36733

Genetic Privacy and Newborn Screening

- Studies have demonstrated feasibility of identifying DNA donors from a public research database using information available from popular genealogy Web sites and other available information.
- Identity of individuals can be ascertained directly from publicly available DNA sequence.
- EMR information is similarly not secure: medical information of 34, 000 patients was leaked from Howard University Hospital and hackers compromised servers of Utah Department of Health and stolen medical information of almost 800,000 individuals.

Ayday et al., @013; arXiv:1306.1264v4

Identifying Personal Genomes by Surname Inference

Melissa Gymrek,[1,2,3,4] Amy L. McGuire,[5] David Golan,[6] Eran Halperin,[7,8,9] Yaniv Erlich[1]*

Sharing sequencing data sets without identifiers has become a common practice in genomics. Here, we report that surnames can be recovered from personal genomes by profiling short tandem repeats on the Y chromosome (Y-STRs) and querying recreational genetic genealogy databases. We show that a combination of a surname with other types of metadata, such as age and state, can be used to triangulate the identity of the target. A key feature of this technique is that it entirely relies on free, publicly accessible Internet resources. We quantitatively analyze the probability of identification for U.S. males. We further demonstrate the feasibility of this technique by tracing back with high probability the identities of multiple participants in public sequencing projects.

Surnames are paternally inherited in most human societies, resulting in their co-segregation with Y-chromosome haplotypes (*1*–*5*). Based on this observation, multiple genetic genealogy companies offer services to reunite distant patrilineal relatives by genotyping a few dozen highly polymorphic short tandem repeats across the Y chromosome (Y-STRs). The association between surnames and haplotypes can be confounded by nonpaternity events, mutations, and adoption of the same surname by multiple founders (*5*). The genetic genealogy community addresses these barriers with massive databases that list the test results of Y-STR haplotypes along with their corresponding surnames. Currently, there are at least eight databases and numerous surname project Web sites that collectively contain hundreds of thousands of surname-haplotype records (table S1).

The ability of genetic genealogy databases to breach anonymity has been demonstrated in the past. In a number of public cases, male adoptees and descendants of anonymous sperm donors used recreational genetic genealogy services to genotype their Y-chromosome haplotypes and to search the companies' databases (*6*–*9*). The genetic matches identified distant patrilineal relatives and pointed to the potential surnames of their biological fathers. By combining other pieces of demographic information, such as date and place of birth, they fully exposed the identity of their biological fathers. Lunshof *et al.* (*10*) were the first to speculate that this technique could expose the full identity of participants in sequencing projects. Gitschier (*11*) empirically approached this hypothesis by testing 30 Y-STR haplotypes of CEU participants in these databases and reported that potential surnames can be detected. [CEU participants are multigenerational families of northern and western European ancestry in Utah who had originally had their samples collected by CEPH (Centre d'Etude du Polymorphisme Humain) and were later reconsented to participate in the HapMap project.] However, these surnames could match thousands of individuals, and the study did not pursue full re-identification at a single-person resolution.

Our goal was to quantitatively approach the question of how readily surname inference might be possible in a more general population, apply this approach to personal genome data sets, and demonstrate end-to-end identification of individuals with only public information. We show that full identities of personal genomes can be exposed via surname inference from recreational genetic genealogy databases followed by Internet searches. In all cases in which individuals were studied who had donated DNA samples, the informed consent statements they had signed stated privacy breach as a potential risk and the data usage terms did not prevent re-identification. Representatives of relevant organizations that funded the original studies were notified and confirmed the compliance of this study with their guidelines (*12*).

As a primary resource for surname inference, we focused on Ysearch (www.ysearch.org) and

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Science
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Identifying Personal Genomes by Surname Inference
Melissa Gymrek *et al.*
Science **339**, 321 (2013);
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Summary and Discussion

- Most children with congenital CMV infection are destined to be normal
  - Reconciling this fact with the ACMG guidelines for screenable disorders will be challenging
  - Appeal to public health benefits
  - More knowledge about the ‘asymptomatic’ child
- Newborn screening has been under attack as a genetic privacy issue
  - Trust
  - Utilitarian ethics
  - Consent
  - Acceptance of information and uncertain future
- More information needed about cost-benefit of early intervention and specifically antiviral therapy (symptomatic vs. asymptomatic)

Disclosure Slide

I do support implementation of universal newborn screening for congenital cytomegalovirus infection

☑ Yes

☐ No


15
35
2
DUCKS
28
51