REPORT OF THE
VIRGINIA DEPARTMENT OF HEALTH

A Study of the Feasibility of Adding Congenital Adrenal Hyperplasia to Newborn Screening Tests

TO THE GOVERNOR AND
THE GENERAL ASSEMBLY OF VIRGINIA

SENATE DOCUMENT NO. 27

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COMMONWEALTH of VIRGINIA

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January 11, 2001

TO: The Honorable James S. Gilmore, III
Governor

THROUGH: The Honorable Claude A. Allen
Secretary of Health and Human Resources

FROM: E. Anne Peterson, M.D., M.P.H.
State Health Commissioner E Anne Peterson, MD, MPH

SUBJECT: Newborn Testing

The report contained herein is pursuant to Senate Bill 699 (2000) which directed the Commissioner of Health to examine the efficacy of certain testing. The Commissioner of Health was requested to examine the issues, costs, and benefits of testing newborns for congenital adrenal hyperplasia (CAH) and to make recommendations to the 2001 General Assembly concerning the requiring of such testing of infants. In conducting this examination, the Commissioner was to consult with pediatricians and other experts and the parents of affected children.

The total cost of the study, including one meeting of the Genetics Advisory Board, survey of physicians and parents, and VDH personnel, equals $50,538.

Executive Summary

In 2000 the General Assembly passed SB 699 (introduced by Senator Ticer) to study whether it is feasible and beneficial to add a test for congenital adrenal hyperplasia (CAH) to the newborn screening tests required of birthing hospitals and health care providers. The Newborn Screening Subcommittee of the Genetics Advisory Board, composed of endocrinologists from four regions of the state and representatives from the Department of General Services, Division of Consolidated Laboratory Services (DCLS), and the Virginia Department of Health (VDH) determined the methodology for this study. VDH conducted a literature review and surveys of pediatric endocrinologists, laboratories and parents of children with CAH. VDH also estimated the cost of adding a test for CAH to the current battery of tests. This study differed from one undertaken by VDH in 1998 because this bill requested the Commissioner to consult with parents of affected children.

CAH is an autosomal recessive genetic disease that causes an enzyme deficiency (most commonly 21-hydroxylase) resulting in an excess of adrenal androgenic hormone production and the inability of the adrenal glands to make other hormones necessary to maintain life. CAH is a continuum of disorders rather than distinct subtypes, which may produce life-threatening complications and incorrect sex assignments on one extreme, or few symptoms and no physical signs on the other. Treatment regimens vary depending on its place on the continuum. The more serious or "classic" forms of CAH may result in high mortality and morbidity if undetected, and can be treated effectively after diagnosis. For these reasons, it appears to be a good candidate for newborn screening.

Each component of the newborn screening program would need to be examined in order to perform comprehensive cost benefit analysis, i.e., screening, initial referral, diagnosis, treatment and follow-up and program evaluation/quality assurance. Several studies have indicated the cost benefit of screening for PKU (similar in incidence to CAH), but no cost benefit analysis of adding CAH to the newborn screening battery of tests has been conducted. However, another approach that has merit is comparing the cost of the doing the screening to doing nothing as a way to assess the cost of morbidity caused by the disease.

In 1988, the US Congress Office of Technology Assessment (OTA) published a review of the effectiveness and costs of newborn screening as compared to no screening. The study included the basic approach, which analyzed the cost of comprehensive screening program for phenylketonuria and hypothyroidism. The OTA analyses concluded that the net health care savings per 100,000 infants screened (using 1996 dollars) was $3.2 million, and that the net health savings per case detected and treated was $93,000. A study by the Texas Department of Health, who has a universal screening program, estimated the cost of diagnosing the six infants found with CAH at $691,000 (1994).

The cost of adding CAH to the newborn screening program includes DCLS; the cost of new instrumentation and reagents ($400,000/year); design, deployment and training on a new newborn screening request form to accompany each newborn sample ($30,000 first year); DCLS staff costs ($140,000), including laboratory technicians and clerical support; and VDH staff costs, nurse for coordination and patient follow-up, and program support technician ($40,000). The total first year cost is $620,000 and ongoing costs are $590,000.

The newborn screening program is funded by fees charged for sample collection kits purchased by providers in hospitals. The costs of adding a CAH kit would be incurred by the NBS Enterprise Fund and would result in an increase in the price per test from the current charge of $16 to $21.

Determining whether adding CAH is cost effective requires an assessment of the many factors that contribute to cost of the disease for parents, the health care system, and taxpayers. Many of the costs are not quantifiable or are difficult to estimate. Therefore, this analysis does not include costs to the family such as transportation to doctor appointments, time missed from work, or the cost of stress and trauma that result from a false positive, medical emergency or infant death. The major direct costs are physician visits, laboratory and hospital costs, including emergency room visits. Estimates on outpatient care from the Texas program and length of stay and hospital costs from Virginia Hospital Information were used to determine costs for Virginia. Using the range of incidence of 1 in 7,000 reported Virginia births versus 1 in 15,000 national births or 6 to 14 cases per year in Virginia, the total direct cost savings estimated to add CAH to newborn screening tests would be approximately $40,128 to $93,632. This calculation does not include that occasional child who is hospitalized and incurs catastrophic expenses.

Given limitations of the data on the cost effectiveness of adding CAH and the absence of specific national guidelines for cost analysis, the Genetics Advisory Board and VDH focused on whether CAH met accepted national criteria for adding newborn screening tests. It also considered the incidence of CAH, current practice in other states, the results of physician and parent surveys, insights from the literature, and the personnel and equipment costs associated with adding the test, in determining whether CAH should be added to the newborn screening tests in Virginia.

The survey of the pediatric endocrinologists showed that two to three percent of the classic CAH patients followed in Virginia were not diagnosed in the newborn period. The survey shows that 14 out of 96,000 live births were diagnosed, resulting in an incidence of 1in 7000, which is twice the national rate for CAH. A review of birth records also found that there have been no reported deaths due to CAH in the last 10 years. Surveys of endocrinologists suggest there are at least 96 patients in Virginia living with CAH.

The state survey by the American Public Health Laboratories (APHL) found that 17 states are screening for CAH; that the average cost for these screens range from 40 cents to three dollars per test; and that the rate of case finding varies from 5 to 11 cases in 100,000 live births.

SB 699 asked for input from parents of children diagnosed with CAH. Not surprisingly, the parents who replied to the survey are supportive of adding CAH to the battery of newborn screening tests. Parents reported that pediatricians needed more education about this condition so that they can quickly recognize symptoms and make referrals to endocrinologists and parent support groups. Many parents reported their child narrowly escaped death because a sudden adrenal crisis was not recognized as such by physicians treating their baby.

There are two policy options to consider in determining whether VDH should add CAH to the newborn screening program.

- One policy option is to amend the Virginia *Code* 32.1-65 to add CAH to those tests currently performed by the Virginia Newborn Screening Program.

Classic CAH meets all of the national criteria for a newborn screening program because it is a reliable, efficient screening test; it is associated with high incidence of illness and life threatening if undetected; and there is an effective treatment to minimize morbidity and mortality. This option would require an additional $620,000 in the first year and $590,000 per year. This cost would be covered by the Newborn Screening Enterprise Fund by increasing the fee per newborn sample from $16 to $21.

- Another policy option is to not add CAH to the newborn screening program at this time.

The cost analysis demonstrates that adding this test may cost more than the cost of identifying these children, as they become ill. There have been no reported deaths due to this condition in ten years and estimated health care costs are less when compared to the cost of establishing and maintaining the CAH newborn screening program. There are no new costs associated with this option.

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I. Literature Review

Incidence and Etiology

CAH is an autosomal recessive genetic disease that causes an enzyme deficiency (most commonly 21-hydroxylase). This enzyme is necessary for the efficient production of two critical adrenal steroid hormones: cortisol, the stress hormone, and aldosterone, the kidney function regulator. Deficient production of these substances causes a hormonal imbalance and triggers an overproduction in the androgens, or male hormones. The clinical presentation of CAH is associated with the severity of the defect and the resultant enzyme activity. It is categorized as either classical or nonclassical.

There is variation among racial and ethnic groups in the classical form. Because of the limited number of screening programs and small numbers of identified cases, the reasons for these differences are unknown. The classical severe form has an estimated worldwide prevalence at birth of 1 in 15,300 people. Texas reports from their data collected over a six-year experience in CAH newborn screening that CAH is less common in African-Americans than in whites or Hispanics. (Therrell, 1998)

Classical CAH exists in two forms: salt-wasting and simple virilizing. It affects the manufacture of the hormone cortisol in the nonsalt wasting form and aldosterone in the salt-wasting form. Cortisol is a hormone which is essential to maintain life and is produced by the adrenal gland, a small organ near the kidney. Cortisol is responsible for maintaining the body's energy supply, blood sugar and control of the body's reaction to stress. An adrenal crisis, or the complete failure to maintain hormonal balance, can result in death. (Therrell 1993, Therrell 1994) Aldosterone is necessary for maintaining a normal balance of salt and water in the body. People with classical CAH are likely to have trouble retaining salt, a condition that can be life threatening. These hormones are necessary to maintain blood pressure, especially during illness or trauma when the body is stressed. A child affected with CAH can go into adrenal crisis if they experience any unusual stressor, such as an infection, injury or surgery.

The excess adrenal androgen production begins in early fetal life in classical CAH-affected infants and causes abnormal growth of girls' clitorises and masculinization of the genital-urinary structures. Affected boys have no genital malformations at birth, but continued androgen excess causes unusually fast body growth. (Therrell 1994, AAP) Therefore, girls with classical CAH are born with masculine-appearing external genitals but with female internal sex organs. Distinction between an enlarged clitoris and small penis can be made by careful examination. Boys with classical CAH look normal at birth so their diagnosis of CAH is sometimes missed.

An infant with the salt-wasting form of CAH may have any or all of the following symptoms within the first few weeks of life: vomiting, poor weight gain, poor feeding, drowsiness, diarrhea and dehydration. Blood tests would reveal a lower than normal level of salt in the blood. The infant may go into shock. Without proper treatment, death can ensue. CAH as an underlying condition contributes to the severity of other illnesses when they occur. Though no deaths have been reported due to CAH in the last 10 years,

there is some concern by physicians and parents of children with CAH that some children have died, but were not accurately diagnosed, identified or that the death certificate did not report the contribution of CAH as a secondary or primary diagnosis. Male newborns with the salt-wasting form of CAH will have no outward physical signs except possible increased pigmentation around the genitals. Female newborns with the salt-wasting form of CAH have ambiguous genitalia, which may make the infant appear partially or very much like a male. (Therrell 1994, APP) It is difficult to clinically differentiate between salt-wasting and simple virilizing forms of CAH because there is an overlapping of symptoms in many children. (Therrell 1994)

Nonclassical CAH-21-hydroxylase deficiency is a milder, nonlife-threatening form of CAH-21 that becomes manifest in later childhood or even young adult life, and is not characterized by ambiguous genitalia in girls. These children do not experience adrenal crisis. Generally, such patients seek medical attention because of premature development of pubic hair, irregular menstrual periods, hirsutism (excessive hair growth), or severe acne. Some people are never symptomatic and only identified because of an affected relative. The frequency of nonclassical CAH is unknown, although it has been reported to occur in up to 3% of individuals in certain groups. The identification of the nonclassical form is not being considered for newborn screening.

Carriers of CAH may have mild forms of the disease. The symptoms may begin at any time in life and may be intermittent. (AAP)

Screening, Diagnosis and Treatment

Knowledge about genetic diseases and advances in biotechnology in recent decades has allowed for inexpensive testing of many medical conditions in newborns. In 1962, Dr. Robert Guthrie introduced a method for screening for phenylketonuria (PKU), a genetic inborn error of metabolism. In 1966, newborn screening for PKU was adopted in Virginia. Since then Virginia has added six other disease conditions, including biotinidase deficiency, phenylketonuria, hypothyroidism, homocystinuria, galactosemia, maple syrup urine disease, and sickle cell disease to a mandated battery of newborn screening tests. (Kunk)

Following screening, CAH can be diagnosed by measuring hormones in a blood sample. This blood test measures cortisol and its hormonal raw material, 17-hydroxyprogesterone (17-OHP). Because of the enzyme deficiency, cortisol is not made and would show very low levels on a blood test. There is a build-up in excess of 17-OHP if the child has the disorder. Regardless of whether the newborn is male or female, early diagnosis and medical treatment of CAH is crucial. Without treatment, these children with the salt-wasting form of CAH will eventually have symptoms which can be life threatening.

Timely detection of CAH can prevent sex misclassification of females with ambiguous genitalia. Early replacement of cortisol and aldosterone has resulted in a sharp decrease in mortality among children with the salt-wasting form of the disorder. Data from newborn screening programs in other states have confirmed the benefits in the

prevention of life-threatening complications and incorrect sex assignments. (Therrell 1998) Whether early treatment significantly improves final height in children with all types of CAH remains unclear.

Currently, the standard medical treatment for CAH consists of replacing the cortisol, aldosterone, and extra salt as necessary. Most CAH-affected children will need glucocorticoid (a cortisol-like steroid medication, e.g., oral hydrocortisol in children). In addition, those who have aldosterone deficiency (salt-wasters) need another drug, fludrocortisone, which acts like the missing hormone, aldosterone, to be able to retain salt. Infants and small children may also receive salt tablets as a dietary supplement, whereas older patients eat salty foods. The nonclassical CAH or milder form of the disease is not life threatening and is frequently undiagnosed. Effectiveness of treatment for nonclassical CAH has not been established.

Newborn screening for CAH due to 21-hydroxylase deficiency became possible with the development of a test sensitive enough to measure 17-OHP in blood collected on filter paper from newborn heel sticks. If added, the test would be performed on all live births in Virginia. The blood sample must be collected after the first 24 hours of life but prior to discharge. The administration of any antibiotics or blood transfusions can alter test results. Newborn weight is necessary to accurately interpret test results. Lower birth weights are associated with a higher percentage of false positive 17-OHP test results.

According to the literature, the 17-OHP screening has a sensitivity (the probability of testing positive if the disease is truly present) of 83-90 percent and a specificity (the probability of testing negative if the disease is truly absent) of 99.2-99.8 percent. The false positive rate is 0.2-0.5 percent. The negative predictive value (the probability that an individual is truly disease-free given a negative screening test) is 99.9 percent. A single screening has been shown to be effective at detecting *all* infants with the most severe (life-threatening) form of the disease. A second screen would pick up infants with milder forms of CAH. It would also increase the number of false positives. Since the effectiveness of treatment of infants with nonclassical CAH has not been established, a second screening will not be cost effective. (Brosnan)

II. Study Methodology and Findings

The Newborn Screening Subcommittee of the Genetics Advisory Board, chaired by a Master's in Public Health geneticist, composed of endocrinologists from each of the four regions of the state and representatives from the Department of General Services, Division of Consolidated Laboratory Services (DCLS), and staff from VDH, determined the methodology for conducting the study.

VDH conducted a literature review, a survey of pediatric endocrinologists in Virginia and the surrounding area of Washington, D.C. and other states, and estimated the cost of adding a test for CAH to the current battery of tests.

Eleven pediatric endocrinologists in Virginia and six in the surrounding area of Washington, D.C. were identified to assist in providing information for the study. It was

assumed that all patients in Virginia with CAH would have been identified and followed by pediatric endocrinologists. A survey tool was sent requesting specific information regarding the number of patients currently being seen in their practice, the number diagnosed after newborn hospital discharge (three-five weeks of age), and the number not diagnosed in the newborn nursery who presented with hyponatremia and/or seizures. They were also requested to provide the number of patients cared for in the past five years and in the past year (see Appendix A for copy of survey.)

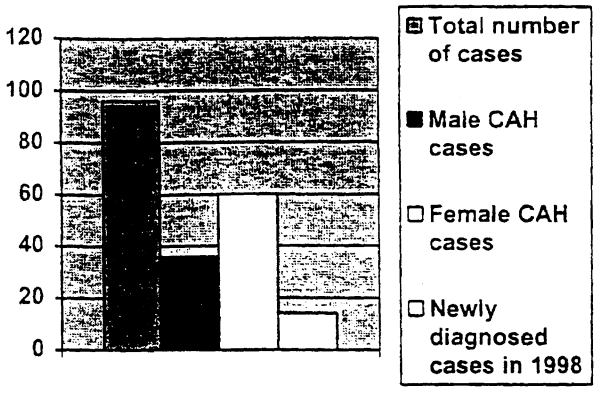
There are no national figures on the cost to diagnose and treat these children. Their initial care at time of diagnosis depends on how sick they are. If a male is detected with salt-losing CAH before they go into a crisis, hospitalization is either brief or not necessary. Once there is a crisis (usually 2-3 weeks of age), there is often the need for intensive care and several days in the hospital. The chronic care involves visits to a specialist 3-4 times a year with $100-$200 of blood tests each visit, as well as medications which are approximately $500 a year. With appropriate follow-up, there should be minimal to no need for hospitalization once the child is stabilized on treatment.

A second survey of other states through the Association of Public Health Laboratories (APHL) was conducted to determine the number of states currently screening for CAH, the methodology being used, the cost of the tests and the number of cases identified (see Appendix B for copy of survey). There are forty laboratories performing newborn screening for fifty states and the District of Columbia.

Survey of Endocrinologists

Of the seventeen pediatric endocrinologists in Virginia and the Washington, D.C. area to whom the survey was sent, ten responded (59 percent), eight of whom were Virginia physicians. The survey revealed that there are 96 patients currently being followed with the diagnosis of CAH (see Table A). Of the males, 24 were diagnosed after the newborn hospital discharge, 14 of which presented with hyponatremia (decreased sodium concentration in blood) and three with seizures. Fourteen new CAH patients were cared for in the past year. This survey reported that most of the cases in Virginia were diagnosed prior to six weeks of age and there was a total of 96 children being served in their practices.

Table A: Estimated Number of CAH Cases in Virginia



In response to the question "Should CAH be added to the current battery of newborn screening tests?" three respondents noted yes, two no and three maybe. One respondent recommended adding CAH screening, and noted that the incidence of CAH, one case in 7,000 live births, appears to be higher than the national incidence. The two respondents who noted that Virginia should not add CAH to the battery of newborn screening believe it is not cost effective, but had no data to support their opinion. The three respondents who said "maybe" expressed concern about the laboratory's capacity to perform the test without too many false positives.

Survey of Other States by the Association of Public Health Laboratories

Forty laboratories in the United States accept blood samples to perform CAH tests. The survey was sent to all of these laboratories and thirty-three responses (83 percent) were received. The survey found that newborn screening for CAH is performed in seventeen states. Only one state program reported that they are considering the adoption of this test. The average cost for these tests range from 40 cents to three dollars per test. Five states use the 17-OHP by Radioimmunoassay method and ten states use the Auto-Delphia method. Only one other state program reported considering adding CAH to their screening program. Cases of CAH found by laboratories range from 5 to 11 cases in 100,000 live births.

Table B: Survey of States Testing for Congenital Adrenal Hyperplasia

State	Year Began Testing	Birth Rate	Test Method	Criteria Used in Evaluating Results	#Cases per Year	Cost	Rate of False Positives	# of Followup Staff
Alabama	1994	60,000	RIA	GA & BW	2	N/D	N/D	N/D
Alaska	1987	10,000	RIA	GA & BW	N/D	$2.00	1.7%	1/2
Florida	1995	188,000	Auto-Delphia	GA & BW	26	$1.90	N/D	N/D
Georgia	1990	110,000	RIA	GA & BW	39	$.40	N/A	0
Illinois	1987	182,000	Auto-Delphia	GA & BW	6	$1.00	N/A	0
Iowa	1990	37,000	Auto-Delphia	GA & BW	35	N/D	0.05	0
Massachusetts	1990	80,000	Auto-Delphia	GA & BW	5	$2-3	3:1	0
Michigan	1993	133,000	Auto-Delphia	GA & BW	31	$2.00	87	N/D
Minnesota	1993	65,000	FIA	BW	N/D	N/D	N/D	N/D
New Mexico	1998	28,000	Auto-Delphia	GA & BW	N/A	$.70	N/A	0
North Carolina	1989	104,000	Auto-Delphia	BW	37	$.57	200	1
Oregon	1985	30,700	RAI	GA & BW	32	$2.00	1.7%	0
Rhode Island	1994	14,000	Auto-Delphia	GA & BW	N/D	N/D	N/D	N/D
South Carolina	1992	50,000	Auto-Delphia	GA & BW	20	$1.00	N/D	N/D
Tennessee	1998	76,000	Auto-Delphia	GA & BW	None	$.70	N/A	1
Texas	1987	335,000	RIA	BW	30	$1.50	N/D	N/D

BW = birth weight
FIA = fluoroimmunoassay
GA = gestational age
N/A = not applicable
N/D = no data
RIA = radioimmunoassay

Survey of Parents

SB 699 requested that the Commissioner consult with parents of affected children. Parents were surveyed by asking physicians to send surveys to their patients with CAH in Virginia and by posting the survey on the Internet message board for parents with children diagnosed with CAH. Dozens of parents described confusion on the part of physicians in diagnosing the problem, many of which resulted in expensive testing for a host of conditions and hospitalization. The most frequently reported symptoms were severe dehydration (19 or 35%) and abnormal appearing genitalia (21 or 38%). Nine out of 54 parents reported that their children were near death at the time of diagnosis. They believe early testing of all newborns would not only reduce medical expenses, but also prevent unnecessary stress and heartache on the part of parents with children with this disease. Parents reported that routine screening would prevent the death of some children who lose salt and go untreated. Parents have support available to them through such organizations as the Congenital Hyperplasia Family Support and Education Network, the Congenital Hyperplasia Support Association, the MAGIC Foundation for Children's Growth and the National Adrenal Diseases Foundation.

III. Costs and Issues in Implementation

The newborn screening program includes five components: 1) screening, 2) initial referral, 3) diagnosis, 4) treatment and follow-up, and 5) program evaluation/quality assurance. Each aspect of the program would need to be examined in order to perform comprehensive cost benefit analysis. Several studies have indicated the cost benefit of screening for PKU, but no cost benefit analysis of adding CAH to the newborn screening battery of tests was found. (Thomason) On the other hand, comparing the cost of the doing the screening to doing nothing has merit in addressing the cost of morbidity caused by the disease. In 1988, the US Congress Office of Technology Assessment (OTA) published a review of the effectiveness and costs of newborn screening as compared to no screening. The study included the basic approach, which analyzed the cost of comprehensive screening program for PKU and hypothyroidism. The OTA analyses concluded that the net health care savings per 100,000 infants screened (using 1996 dollars) was $3.2 million, and that the net health savings per case detected and treated was $93,000. (AAP) A study by the Texas Department of Health, who has a universal screening program, estimated the cost of diagnosing the six infants found with CAH at $691,000 (1994).

The recent report of the Newborn Screening Task Force in May 1999 in *Serving the Family from Birth to Medical Home - Newborn Screening: A Blueprint for the Future*, calls for a national agenda on state newborn screening programs that would include assessing the costs incurred by the programs. (AAP)

Table C: Estimated Cost of Adding CAH to the Virginia Newborn Screening Program

Cost Items	Initial Year	Yearly
Diagnostic tests 50 x $200 (cost to insurance or patient)	$10,000	$10,000
Instrumentation (cost to Newborn Screening Program Enterprise Fund)	$400,000	$400,000
Ongoing personnel costs (cost to NSPEF)	$180,000	$180,000
Education of providers, redesign and printing of collection forms (cost to NSPEF)	$30,000	0
Total	**$620,000**	**$590,000**

There are important issues that must be considered in adding CAH to the tests used to screen newborns in Virginia. There will be costs associated with the follow-up on all positive tests. Based upon the reports of other states conducting NBS for CAH and case finding rates published in the literature, it is reasonable to expect between 150 to 200 positive results per year. Therefore, the total cost of rescreening all newborns with an initial positive screen would be $450.00. Using the data from the Texas program, approximately one-third or 50 of these re-screens would need the diagnostic testing. In Virginia, the Medicaid reimbursement rate for 21-hydroxylease deficiency testing is $97.00. Considering the need for an additional office visit, review of test, and follow-up, the estimated cost of diagnosing CAH is $200.00 per case, or 200 x 50 cases for a total of $10,000.

Because the baby's weight at the time of collection affects the specificity of the test, it needs to become a required field on the laboratory form. Therefore, the laboratory will be required to modify the collection device. The current NBS laboratory computer system has no instrumental interfacing capabilities and could not match CAH raw data against the factors necessary to provide interpretation of results. Based on information provided from other NBS programs, without this capability, the number of false positives would be very high and follow-up would be either difficult or impossible. Therefore, DCLS newborn screening laboratory would need a new rental agreement for computer hardware and software, instrumental interfacing of the NBS computer system, and modification of the collection and processing of data collected at the time of birth.

To add CAH, the annual laboratory cost of reagents and instrumentation is estimated at $400,000 per year. In addition, ongoing staff costs for the DCLS personnel are approximately $140,000 per year. Additional cost would include VDH personnel in the form of one part-time nurse coordinator and one part-time support technician at approximately $40,000 total. The nurse will coordinate educational aspects and parent and provider contact within the program. An additional $30,000 is needed in the first year to cover printing of updated laboratory and educational materials, travel costs for hospital and provider in-services, and redesign of the demographic portion of the NBS collection device. Total first year cost would be $620,000 and ongoing costs would be $590,000.

Presently, the newborn screening program is supported by fees charged for the collection kits used by providers in hospitals. The costs would be incurred by these funds, NBS Enterprise Fund, but would translate into an increase in the NBS price per test. Each year, approximately 120,000 tests are done, which would calculate the cost of each CAH test to be $5. To cover the cost of adding this test, an increase in the NBS fee at a minimum from the current charge of $16 to $21 per test will be required.

Estimating cost effectiveness includes assessment of multiple factors contributing to those costs, many of which are difficult to obtain. This cost analysis does not include resource cost such as transportation or time away from work for the family or the psychological costs that result from a false positive or infant death. The major direct cost factors are physician visits, laboratory and hospital costs, including emergency room visits. The Texas program estimated $719 of total cost per case was incurred in those children not screened at birth and diagnosed later upon onset of symptoms. The Texas program also estimated an average hospital cost of $3,871 per undiagnosed case of CAH. Based on hospital discharge data from Virginia Hospital Information, it is estimated there were 9 infants (under 42 days of age) with CAH as a primary or secondary diagnosis in 1998 and 1999. The average length of stay for these infants was 4.5 days and the average hospital cost was $5,969. Using the range of incidence of 1 in 7,000 Virginia births versus 1 in 15,000 national births or 6 to 14 cases per year in Virginia, we added the total physician units ($719) to the average Virginia hospital cost ($5,969). Therefore, the total direct cost savings estimated in Virginia to implement a CAH newborn screening would be approximately $40,128 to $93,632. This calculation does not include that occasional child who experiences the catastrophic hospitalization. One Virginia parent reported that

in 1993 their child almost died before diagnosis was made and had a hospital bill of more than $30,000.

IV. Discussion and Policy Options

There are two policy options to consider in determining whether VDH should add CAH to the newborn screening program.

- One policy option is to amend the Virginia *Code* 32.1-65 to add CAH to those tests currently performed by the Virginia Newborn Screening Program.

Classic CAH meets all of the national criteria for a newborn screening program because it is a reliable, efficient screening test; it is associated with high incidence of illness and life threatening if undetected; and there is an effective treatment to minimize morbidity and mortality. Evident from the parent survey and experiences reported by other states, there is need for general awareness and education for the providers of infant health care. Adding CAH to the newborn screening program will provide that education so that children will be identified and treated quickly. VDH, in collaboration with DCLS, would provide that training to health care providers. The Genetics Advisory Board confirms that classical CAH meets the criteria for a disorder suitable for newborn screening in Virginia and recommends to do so if fees are raised to cover the costs.

- Another policy option is to not add CAH to the newborn screening program at this time.

The cost analysis demonstrates that adding this test may cost more than the cost of identifying these children when they become ill. There have been no reported deaths due to this condition in ten years and estimated health care costs are less when compared to the cost of establishing and maintaining the program. Ideally, adding CAH to the newborn screening program would prevent the hospitalizations, but that was not the experience in the Texas program. Complete prevention of hospitalization will be impossible even though a timely and efficient program could decrease the length of stay and the number of hospitalizations. With the event of major advances in genetic medicine recently, there may be other conditions which would readily lend themselves to newborn screening. DCLS and VDH should continue to explore ways to design the new DCLS computer system so that screening tests can be easily added in a cost effective manner.

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Appendix

Appendix A Survey of Endocrinologists

Appendix B Survey of States

Appendix C Survey of Parents

Appendix A
Survey for the Addition of
Congenital Adrenal Hyperplasia to Newborn Screening

Pediatric Endocrinologist: _____
Address: _____
_____

Telephone: _____

Fax: _____

E-mail: _____

1. Number of patients with CVAH currently being followed by you? _____

2. Number of male patients with CVAH currently being followed by you? _____

3. Number of patients with CVAH currently being followed by you who were diagnosed after newborn hospital discharge (3 weeks to 5 years of age)? _____

4. Number of patients who were not diagnosed in newborn nursery who presented with hyponatremia? _____ seizures?_____

5. Number of new CVAH patients you have cared for in the past year? _____
Past five years? _____

6. Do you believe that CVAH screening should be added to the current battery of newborn screening tests? _____ Why or why not?

Comments:
_____
_____
_____
_____

Appendix B – Survey of States

During the 1998 Virginia legislative session, a bill was passed (HJR 183) which mandated the newborn screening program to study whether requiring second infant screenings for congenital hypothyroidism would be beneficial. We were also asked to consider the addition of congenital adrenal hyperplasia. We would very much like to hear from other states. Please respond to the questions in study #1 and/or study #2 as appropriate. We would greatly appreciate a response **within 2 weeks**. You may e-mail me at arogers@vdh.state.va.us or fax the information to Arlethia Rogers at (804) 371-6032. The mailing address is Virginia Department of Health, Division of Women's and Infants' Health, 1500 East Main Street, Room 135, Richmond, VA 23219. Thank you in advance for your response.

Questions for the Congenital Hypothyroid **Study #1**:

1. What is the number of births for your state per year?
2. For what disorders are you currently screening?
3. Are you doing second screenings? If no, go to **Study #2**. If yes, continue.
4. What is the cost per test? Is it cost-effective?
5. When did you start to do second screenings?
6. Is the complete battery of tests screened for repeated on second screenings?
7. What is the percent of cases found on second screenings?

Questions for the Congenital Adrenal Hyperplasia **Study #2**:

1. When did screening for CAH begin?
2. What test methodology is used for CAH?
3. What is the cost per test of CAH screening?
4. What is the total number of cases found and the rate?
5. What is the rate of false positives?
6. What criteria are used in evaluating results?
7. How many follow-up staff are dedicated for CAH?

Appendix C

October 3, 2000

Dear Parent or Guardian:

The Virginia Department of Health has been directed by the Virginia General Assembly to study the feasibility of adding congenital adrenal hyperplasia (CAH) to the tests which are done by heelstick in the newborn period. About sixteen states currently offer this test but Virginia does not at present. Because of your past experience with CAH, you are in a unique position to tell us whether newborn screening would have benefited your child if it had been available when your child was born. We would appreciate your answering the following questions. This survey is confidential.

1) Name of Child: _____ 2) Date of Birth: _____ 3) Sex: _____

4) Age of your child when diagnosis was made (☐ check if approximate) _____ days _____ weeks

5) What made your doctor(s) first suspect that your child had CAH? Please check all that apply.

___ Abnormal appearing genitals
___ severe dehydration (salt-losing crisis)
___ precocious puberty
___ a previous child had the same diagnosis

6) If you had learned of your child's diagnosis by newborn screening at the age of 10 days, would it have made a difference in the care of your child or your ability to deal with this difficult diagnosis? Please check all that apply.

___ The diagnosis was made before 10 days so it would have made no difference

___ The diagnosis was made after 10 days and it would have made no difference because

_____

_____

___ The diagnosis was made after 10 days but knowing the diagnosis earlier would not have made much of a difference.

7) Other thoughts and comments

_____

_____

Thank you for your participation in this survey. We do appreciate it very much.

Sincerely,

Paul Kaplowitz, M.D.
Endocrine Consultant
Newborn Screening Program

Appendix D

SENATE BILL NO. 699
Offered January 24, 2000
A BILL to direct the Commissioner of Health to examine the efficacy of certain testing.

Patrons-- Ticer, Byrne, Edwards, Howell, Lambert, Marye and Miller, Y.B.; Delegates: Darner, Hull and Moran

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Referred to Committee on Education and Health

Whereas, congenital adrenal hyperplasia (CAH) is a developmental disorder that is difficult to diagnose; and

Whereas, the symptoms of congenital adrenal hyperplasia are gradual, but can rapidly result in the death of a newborn child; and

Whereas, death can be prevented by replacing the substance that the children do not produce; and

Whereas, there is a simple test for this condition that could result in saving the lives of many children; and

Whereas, however, some issues relating to false positive test results among premature infants must be resolved; now, therefore

Be it enacted by the General Assembly of Virginia:

1. *§ 1. Commissioner directed to examine the efficacy of certain testing. The Commissioner of Health shall examine the issues, costs, and benefits of testing newborns for congenital adrenal hyperplasia (CAH) and shall make recommendations to the 2001 General Assembly concerning the requiring of such testing of infants. In conducting this examination, the Commissioner shall consult with pediatricians and other experts and the parents of affected children.*

Go to (General Assembly Home)