These newborn screening fact sheets were developed by the Committee on Genetics of the American Academy of Pediatrics with considerable assistance and consultation from many individuals. The fact sheets were not designed to advocate specific newborn screening tests but rather to inform pediatricians about these tests. Many states are considering addition of new tests to their screening batteries, whereas others may be reviewing their current screening panel to reduce the number of disorders for which tests are offered. This information should assist pediatricians in developing appropriate positions based on the needs of their patients and of their geographic regions.

In addition, the information in these fact sheets may assist the pediatrician in understanding the individual tests, their characteristics, and their strengths and weaknesses. Such information is important for evaluating policies and procedures.

Our knowledge base regarding newborn screening is changing rapidly and there are numerous areas of controversy. We have attempted to provide a consensus viewpoint, but it must be recognized that experts in this field do not always agree. Pediatricians who desire additional information should contact the specialists in their region or those involved at a national level. Brief bibliographies have been provided to assist the clarification of some of these points.

These fact sheets will require revision in the future. Your comments and suggestions will be appreciated.

NOTE ON COST: The costs quoted here are those for the screening tests in a regionalized laboratory. There is a program cost of approximately $1 to $2 for specimen handling, administration, equipment depreciation, and overhead that has been traditionally ascribed to phenylketonuria. These costs will vary depending on size and scope of the program. These cost figures do not include the total system's cost for newborn screening, including education, confirmation, follow-up, and management.

GENERAL REFERENCES
Genetic Screening—Program, Principles and Research. Washington, DC, National Academy of Sciences, 1975

BIOTINIDASE DEFICIENCY
Autosomal recessive disorder of biotin recycling that leads to multiple carboxylase deficiency. Signs and symptoms include convulsions, dermatitis, alopecia, ataxia, hearing loss, developmental abnormalities, and organic acidemia with acute metabolic decompensation resulting in coma. Death may occur.

DISEASE CHARACTERISTICS
Incidence: 1:70,000 (confidence interval for relatively limited series 1:27,000 to 1:277,000).
**Racial/Ethnic Variability:** Unknown.

**Sex Ratio:** M = F; no cases known in blacks or Asians.

**Severity/Variability Without Screening**

Mortality: Has occurred during acute metabolic decompensation, but frequency is unknown (4/20 reported).

Developmental Disabilities: Based on data from 35 patients: Age at onset of neurologic signs and symptoms has varied from 2 weeks to 3 years. It is unknown whether completely asymptomatic persons exist. Convulsions, ataxia, hypotonia, developmental delay, hearing loss, optic atrophy, and/or decreased vision may occur. Treatment after diagnosis leads to some improvement. Hearing loss is not resolved. Ultimate psychomotor outcome with postsymptomatic treatment is unknown.

Physical Disabilities: Based on 35 patients: Age at onset of symptoms has varied from 7 weeks to 3 years. Rash, conjunctivitis, alopecia, and fungal infections may be seen. Symptoms are mild in at least some patients. It is unknown whether asymptomatic persons exist. Some abnormalities are reversible with treatment.

Potential for Symptomatic Diagnosis: Nonspecific features may result in delayed or missed diagnosis. Organic aciduria has led to diagnosis in many cases but was absent in 15% of cases reviewed by Wolf et al.

Variability: Undetermined. Some untreated affected individuals have had only mild neurologic symptoms at 3 years of age.

Mortality: None reported (12 cases worldwide).

Developmental Disability: Longest follow-up is 27 months. All 12 screened patients are asymptomatic after treatment.

Physical Disability: Longest follow-up is 27 months. All 12 screened patients are asymptomatic while being treated.

Variability: Inter- and intrafamilial clinical variability is seen. No cases have been identified by screening and left untreated to evaluate natural history, although mild symptoms or biochemical abnormalities have been identified prior to treatment. It is unknown whether completely asymptomatic persons with variant forms exist.

**Possible Interventions**

Treatment: Oral biotin has reversed physical and some neurologic findings. Reversal and/or prevention of developmental delay is unclear. Postsymptomatic treatment may not reverse hearing loss and/or optic atrophy and has not improved retardation in some cases. Optimal dosage of biotin is unknown. Hazards of biotin treatment are unknown but treatment with 10 mg/d has been well tolerated to date. Treatment is relatively inexpensive (estimate $25 to $100/yr). Biotin is available from Hoffmann-LaRoche, Nutley, NJ. Some biotin purchased at pharmacies or health food stores cannot be used to treat these children; its use has been associated with clinical deterioration.

Hazard Avoidance: None known.

Genetic Counseling: Autosomal recessive. Potential for prenatal diagnosis has been demonstrated but not yet accomplished. Prenatal treatment is possible but probably unnecessary. Long-term prognosis is unknown.

**SCREENING TEST CHARACTERISTICS AND CONFIRMATION**

**Type of Test:** Colorimetric assay (for biotinidase) on dried blood spot. Should be interpreted within 30 minutes of developing. Reagents are commercially available. Affected infants and children have 0% to 3% of normal adult activity.

**Cost:** Approximately $0.25 to $0.50.

**Stability of Specimen:** Samples stored for >18 months at room temperature or higher had no detectable activity. Activity was detected in samples <18 months old. Samples analyzed 1, 30, and 60 days after collection were stable. Specimens are stable frozen at −70°C for 3 years.

**Field Testing:** Pilot study performed using samples obtained by the Commonwealth of Virginia but analyzed in research laboratory. Other states and countries have readily set up the assay and are screening.

**Confirmation:** Both colorimetric and a more sensitive radioassay of serum are available to confirm screening results. Based on families studied to date, heterozygotes can be separated from affected and normal individuals with 95% accuracy.

**Accuracy of Screening Test**

- Sensitivity: Unknown.
- Specificity: 0.98 false-negative results may occur with sulfonamides.

**SYSTEM CHARACTERISTICS**

**Timing:** Optimal timing for testing is unknown. Enzyme deficiency has been demonstrated in cord blood; therefore, any specimen obtained after birth...
is anticipated to be adequate. Symptoms have not developed in most patients before 2 months of age, but one was symptomatic at 3 weeks. Thus, rapid turnaround may be needed. Mean age at onset of symptoms is 5 to 6 months.

Coordination: Could be incorporated into present systems.

Public Awareness/Education: Awareness is minimal. Local areas adopting screening may provide educational materials.

Physician Awareness/Acceptance: Recently described; awareness limited.

ONGOING STUDIES: Pilot screening program at Medical College of Virginia, Dr Barry Wolf. Pilot studies now in process in numerous countries and planned or underway in 18 states in the United States. Follow-up of screening cases is in progress.

Research Value of Screening: High. Information is needed concerning incidence, natural history, efficacy of treatment (including evaluation of older, previously symptomatic patients), parameters for optimal treatment, and heterogeneity of disorder.

Hazards and/or Problems Related to Screening: Postsymptomatic treatment may be as effective as presymptomatic treatment in some cases. Risks of treatment are unknown, but no complications have been reported to date. Oldest known patients are 11 to 12 years old; ie, long-term outcome is unclear.

RECOMMENDED READING

BRANCHED CHAIN KETOACIDURIA—MAPLE SYRUP URINE DISEASE (MSUD)

Autosomal recessive disorder of branched chain ketoacid decarboxylation resulting in high serum levels of leucine, isoleucine, valine, and their corresponding ketoacids, lethargy, irritability, and vomiting progressing to coma, and death if untreated, develop in affected individuals.

DISEASE CHARACTERISTICS

Incidence: 1/250,000 to 1/300,000.

RACIAL/ETHNIC VARIABILITY: US populations (mixed) 1/250,000 to 1/300,000. Occurrence may be more common in black and Asian populations.

Sex Ratio: M = F.

Severity/Variability Without Screening

Mortality: Lethal in classical form, usually in first month, if unrecognized and untreated.

Developmental Disabilities: Symptomatic patients treated after diagnosis usually have irreversible retardation. Treatment prior to 12 days of life has resulted in normal intelligence in four cases.

Physical Disabilities: Spastic quadriaparesis and poor physical growth are common.

Potential for Symptomatic Diagnosis: High. Should be considered in any infant with severe acidosis in the first ten days of life. Odor of the urine is characteristic.

With Screening and Treatment

Mortality: All deaths cannot be prevented. At least one infant died at nine days of age, one day before newborn screening results were reported. Death within the first 2 weeks is not uncommon, and about ½ of infants have died before dietary therapy could be instituted. Some patients die suddenly at older ages despite therapy.

Developmental Disability: Age and neurologic symptoms at time of institution of therapy (as well as adequacy of control) affect outcome. Minority of patients have normal intelligence.

Physical Disability: Some screened and treated patients have no disability.

Variability: Variant forms exist including an intermittent form and an intermediate form. Some of these will be detected by screening; others may not be detected. Need for treatment is variable.

Possible Interventions

Treatment: Restriction of branched chain amino acid intake requires frequent monitoring; must be continued indefinitely. Commercial formula is available, but intake of branched chain amino acids must be individually titrated. Nutritionist and specially trained physician must coordinate therapy. Cost is great.

Hazard Avoidance: Dietary only.

Genetic Counseling: Autosomal recessive. Prenatal diagnosis is available.
SCREENING TEST CHARACTERISTICS AND CONFIRMATION

Type of Test: Bacterial inhibition assay for leucine, using dried blood spot, obtained by heel puncture.

Cost: Approximately $0.50 when superimposed on phenylketonuria screening program which also uses bacterial inhibition assay.

Stability of Specimen: Short-term excellent; presumed excellent at −70°C but limited information under special or ambient conditions.

Field Testing: Completed.

Confirmation: Quantitative measurement of leucine, isoleucine, valine; presence of alloisoleucine in serum; enzymatic assay in research laboratories.

Accuracy of Screening Test

Sensitivity: Limited information but dependent on age at testing.

Specificity: High (≥99.9%); dependent upon individual program.

SYSTEM CHARACTERISTICS

Timing: Results must be available in less than 2 weeks; thus, the specimen must be obtained as early as possible. Affected infants have had elevated leucine levels by four to 14 hours of age. Presence of alloisoleucine was first detected at 14 hours.

Coordination: May be incorporated into existing programs. Rapid turnaround time is necessary.

Follow-up: Specialized care, including ability to monitor amino acids, provide nutritional assessment and planning, provide hospitalization and intensive care when necessary.

Public Awareness/Education: Poor.

Physician Awareness/Acceptance: Awareness limited. Aggressive education of physicians with emphasis on early clinical diagnosis is important even with a screening program, because of rapidity of onset (Clow et al).

ONGOING STUDIES: Programs continue to evaluate effectiveness of screening.

RESEARCH VALUE OF SCREENING: Moderately high. Information needed: (1) Ethnic variation in incidence of classical form and variants, (2) long-term prognosis, (3) management at different ages, (4) possibilities for rapid turnaround time, and (5) efficacy of screening at different ages (ie, 24 hours v later).

HAZARDS AND/OR PROBLEMS RELATED TO SCREENING: Infants often damaged by time identified; risk for sudden death; costliness of treatment; heightened clinical acumen may be most important in preventing morbidity.

RECOMMENDED READING


CONGENITAL ADRENAL HYPERPLASIA (CAH)

21-Hydroxylase deficiency accounts for 90% to 95% of syndrome and can be detected by neonatal screening. This is an inborn error of steroid biosynthesis that may produce ambiguous genitalia in girls and salt-losing crises. Disease is transmitted by autosomal recessive gene.

Disease Characteristics

Incidence: 1:12,000.

Racial/Ethnic Variability: White, 1:12,880; Japanese, 1:15,000; Yupik Eskimo, 1:680; Italian, 1:5,500 to 1:10,000.

Sex Ratio: Theoretically M = F. In clinically detected cases, F > M because of masculinization of the female fetus.

Severity/Variability Without Screening

Mortality: Life-threatening adrenal crisis in newborn period (mortality 9%).

Developmental Disabilities: Usually absent but may occur from salt-losing crisis and shock.

Physical Disabilities: Masculinization of female genitalia may be present at birth and result in incorrect sex assignment. Dehydration and vascular shock is common. Adult sexual dysfunction has been reported. Excessive androgenic steroids can result in precocious puberty in boys and masculinization of girls. Androgenic compounds also cause...
accelerated early growth with premature fusion of epiphyses and ultimate short stature.

Potential for Symptomatic Diagnosis: Should be high, but studies show that clinical diagnosis is poor despite ambiguous genitalia and other signs of virilization.

Variability: In severe forms, adrenocortical insufficiency, salt-losing crises, and ambiguous genitalia are seen in female patients. Those with partial forms have adequate but restricted synthesis of cortisol and aldosterone. Patients are able to respond to all but severe stress: not salt losing. Virilization and ambiguous genitalia occurs in girls; early postnatal virilization occurs in boys.

**With Screening, Diagnosis, and Treatment**

Mortality: Reduced substantially but frequency is unknown because of early-onset, salt-losing crises, which may occur before screening results are available. No patients to date have been in severe crisis when screening results were available.

Developmental Disabilities: Should be reduced because of early treatment.

Physical Disabilities: Early diagnosis should lead to correct sex for rearing, eliminate problems of precocious puberty, masculinization, accelerated growth, and later malignancy. Risk of adrenal crisis with stress is still present.

**Possible Interventions**

Treatment: Endocrinology consultation is needed. Treatment with glucocorticosteroids serves the dual purpose of replacing cortisol and suppressing excessive ACTH production. Patients with “salt losing” and elevated plasma renin activity must receive high salt intake and mineralocorticoid therapy in addition to hydrocortisone. Enlarged clitoris of female infants often requires surgical correction, usually between 6 and 12 months of age.

Hazard Avoidance: Analogues of hydrocortisone or cortisone effective in suppressing adrenal androgens but may be too potent in growth suppression; therefore, they are not recommended in the newborn and young child with congenital adrenal hyperplasia.

Genetic Counseling: Autosomal recessive with 25% risk for siblings. Prenatal diagnosis is possible with DNA analysis for identification of 21-hydroxylase deficiency (by chorionic villus sampling within first trimester and by hormone measurement and HLA typing and additional DNA studies by amniocentesis in second trimester). Intrauterine treatment early in first trimester may prevent masculinization of female fetus. HLA typing and DNA studies may allow detection of carriers in families with affected child.

**SCREENING TEST CHARACTERISTICS AND CONFIRMATION**

**Type of Test:** Enzyme immunoassay (EIA)/radioimmunoassay (RIA) for measurement of 17-hydroxyprogesterone (17-OHP) in 21-hydroxylase deficiency. Filter paper/disc impregnated with capillary blood and dried, obtained by heel puncture.

**Cost:** $1.48 per screening test (Alaska study); $1.63 per screening test (Italian study). Cost decreases as volume increases.

**Stability of Specimen:** No decomposition of 17-OHP for as many as 30 days in blood dried on filter paper and blood stored at room temperature.

**Field Testing:** Several pilot studies completed. Samples can be transported by mail. Sample collection is easy; little blood is required.

**Confirmation:** Quantitative measurement of plasma 17-OHP; available from many commercial laboratories.

**Accuracy of Screening Test**

Sensitivity: >95%.

Specificity: Cross-reaction of steroid compounds related to 17-OHP depends on antiserum used in radioimmunoassay of steroids. Recall rate: 0.05% to 0.8%.

**SYSTEM CHARACTERISTICS**

**Timing:** Important to screen early, process quickly, and have rapid follow-up. Premature infants may have false-positive test results. Optimal testing is between ages 48 and 72 hours.

**Coordination:** Convenient to carry out in same laboratory that screens for phenylketonuria and hypothyroidism.

**Follow-up:** Pediatric endocrinologist or private physician with endocrinology consultation.

**Public Awareness/Education:** Limited general knowledge.

**Physician Awareness/Acceptance:** Simple, inexpensive screening available, but this is not well known. Education of health professionals regarding congenital adrenal hyperplasia testing of female newborns with ambiguous genitalia is of paramount importance in all populations. Without screening, diagnosis is difficult in male newborns unless they become symptomatic.
ONGOING STUDIES: Pilot screening programs in progress in Alaska, Japan, Italy, France, Scotland, and New Zealand; completed in Washington state.

RESEARCH VALUE OF SCREENING: Establish true incidence figures. Determine extent to which clinical outcome is improved by early diagnosis and treatment.

HAZARDS AND/OR CONCERNS RELATED TO SCREENING: Effect of screening on prognosis is unknown. Number of false-positive results ranges from 0.2% to 0.5% depending upon the cutoff level chosen.

RECOMMENDED READING

CONGENITAL HYPOTHYROIDISM

Inadequate production of thyroid hormone which may be due to a number of causes including endemic cretinism, agenesis or ectopic thyroid gland, genetic disorders of thyroid hormonogenesis, hypopituitarism, etc. Patients who are not identified and treated promptly suffer mental retardation and variable degrees of growth failure, deafness, and neurologic abnormalities as well as classical hypometabolic symptoms of hypothyroidism.

DISEASE CHARACTERISTICS

Incidence: 1:3,600 to 1:5,000 in the United States from screening; 1:3,000 in Europe; 1:6,600 to 1:7,300 in Sweden by clinical diagnosis; 1:5,700 in Japan.

Racial/Ethnic Variability: Considerably less in black populations (1:17,000 in Georgia, 1:10,000 in Texas); 1:2,700 in Hispanic populations.


Severity/Variability Without Screening

Mortality: May be underestimated because of failure of diagnosis. In one study, 3/141 patients died. Increased mortality in retarded patients may be related to institutionalization.

Developmental Disabilities: Varies in different studies. Based on approximately 800 patients in the literature, mean IQ = 80. Of 250 patients with reported test results, 67% had IQ <85, 40% had IQ <70, and >19% had IQ <55. Other neuropsychologic problems are common. Degree of developmental disability is probably different for different types of hypothyroidism.

Physical Disabilities: May include poor growth, goiters, low metabolic rate, constipation, poor appetite, poor peripheral circulation, bradycardia, and myxedema. More than 95% of infants with sporadic hypothyroidism show such minimal signs at birth that the diagnosis is missed.

Potential for Symptomatic Diagnosis: Clinical signs of hypothyroidism may not appear until the infant is several months of age or older. Infants with early clinical findings seem to have higher incidence of developmental disabilities. Finding of higher incidence from screening programs than from clinical surveillance suggests that cases may be missed.

Variability: Ultimate IQ is probably affected by type of hypothyroidism, severity of deficiency, duration of deficiency before treatment is started, presence of prenatal deficiency, and adequacy of treatment.

With Screening, Diagnosis and Treatment

Mortality: No excess expected.

Developmental Disabilities: Contradictory results from large studies. New England Congenital Hypothyroidism Collaborative study showed normal IQ, visual motor integration, and neuropsychologic profiles when compared with control values. Quebec study showed normal developmental quotients but significantly lower scores than control values.

Physical Disability: None with treatment.

Variability: Neither follow-up study has shown correlation with any disease-related factors except adequacy of treatment (compliance).

Possible Interventions

Treatment: Oral levothyroxine at a dosage to produce thyroxine (T4) concentration in upper half of normal range. Consultation with endocrinologist may be helpful.

Hazard Avoidance: None known.

Genetic Counseling: Depends upon diagnosis of etiology of the hypothyroidism. Dyshormonogene-
sisis occurs most commonly as a result of autosomal recessive genetic conditions. Other causes may also have familial basis in part. Etiologic testing requires scanning and sometimes other studies.

**Screening Test Characteristics and Confirmation**

**Type of Test:** Radioimmunoassay for T₄, thyroid-stimulating hormone (TSH), or both. North American programs generally screen using T₄ values followed by TSH on the lowest 5% to 10%. Use of TSH primary screening is usual in Europe and Japan. Simultaneous determination of both T₄ and TSH is optimal. Nonisotopic enzyme immunoassays have been developed for both TSH and T₄. Use of simultaneous enzyme immunoassay methods should allow less expensive T₄ and TSH testing. Each type of test has been adapted for use with dried filter paper blood spots.

**Cost:** Average for radioimmunoassay $1.50 per test.

**Field Testing:** Complete. Screening now occurs in all 50 states.

**Confirmation:** Quantitative measurement of T₄ and TSH. Thyroid-binding globulin level and free T₄ value is low and TSH is abnormal. Response to thyrotropin-releasing hormone is rarely needed to investigate secondary v tertiary hypothyroidism. Radioactive scanning is necessary to identify the etiology of the hypothyroidism. Repeated testing may be necessary to identify transient hypothyroidism. This testing is available through most clinical laboratories.

**Accuracy of Screening Test**

Sensitivity: Depends upon cutoff used, screening methods, and age of infant. Approximately 6% to 12% of cases are detected only by second screening at 2 to 6 weeks of age. True biologic false-negative test results account for about 11% of missed cases. Primary TSH screening misses secondary or tertiary hypothyroidism.

Specificity: Depends upon tests and cutoffs used. T₄ alone has low specificity. T₄ followed by TSH and, when indicated, thyroxine-binding globulin, reverse triiodothyronine, or free T₄ produces high specificity. Recall rates vary from 0.04% to 0.05%.

**SYSTEM CHARACTERISTICS**

**Timing:** Newborn older than 12 hours for T₄ testing; seven to ten days for primary TSH testing. Retesting of a second sample for T₄ has led to identification of as many as additional 6% to 12% of cases (1/25,000).

**Coordination:** Commonly provided through state departments of health.

**Follow-up:** Usually by private pediatrician with or without pediatric endocrine consultation.

**Public Awareness/Education:** Provided at the time of the infant's birth. Brochures for parents may be available before or after delivery.

**Physician Awareness/Acceptance:** Provided by state programs, regulations, and/or law. Routine mandated screening may lead to less efficient diagnosis of missed symptomatic patients because clinician incorrectly assumes that disorder has been definitively ruled out.

**ONGOING STUDIES:** Long-term outcome. Incidence of transient disease and optimal diagnostic studies and management.

**RESEARCH VALUE OF SCREENING:** Study of etiology, transient disease, hypothyroidism in premature infants; improved testing methods.

**HAZARDS AND/OR PROBLEMS RELATED TO SCREENING:** Decreased vigilance for clinically asymptomatic patients. Most common neonatal signs are prolonged jaundice, constipation, and umbilical hernia. Discriminatory educational placements (occurred in New England). Overtreatment with resultant increased intracranial pressure and/or craniostenosis. Increased anxiety about premature infants who are at increased risk for true transient hypothyroidism as well as low T₄ levels with euthyroidism and low thyroxine-binding globulin levels.

**RECOMMENDED READING**


Layde PM, Von Allmen SD, Oakley GP: Congenital hypothyroidism control programs: A cost benefit analysis. JAMA 1979;241:2290-2292


CYSTIC FIBROSIS

Disorder with autosomal recessive inheritance that is characterized by generalized disturbance in exocrine function.

DISEASE CHARACTERISTICS

Incidence: White, 1/2,000 average; heterozygote, 1/22.

Racial/Ethnic Variability: Increased in northern Europeans; decreased in American blacks.

Sex Ratio: M = F.

Severity/Variability Without Screening

Mortality: Ten percent of neonates with cystic fibrosis (CF) have small bowel obstruction due to meconium ileus. Neonates and infants have 13% mortality from malabsorption and malnutrition. In second to fourth decades, death results from obstructive pulmonary disease and infection. Mean survival is now 22 years.

Developmental disabilities: Rare; normal intelligence.

Physical Disability: Poor growth and chronic respiratory and digestive disorder.

Potential for Symptomatic Diagnosis: Good with meconium ileus; should be good for patient with malnutrition and pulmonary problems but frequently considerable delay occurs.

Variability: Heterozygotes have no recognizable clinical symptoms. No characteristic pattern regarding severity of the disease. Different homozygote family members can display mild or severe disease. Wide spectrum in natural history of this disorder.

With Screening and Treatment

Mortality: Conflicting study results with early intervention, but there is suggestion of reduced morbidity and mortality from malnutrition in infancy.

Physical disabilities: Impact of newborn screening unknown. Early initiation of appropriate management may reduce nutritional and pulmonary disability.

Possible Interventions

Treatment: Improved parenteral and oral nutrition, fat-soluble vitamin supplements, predigested formula, and improved, pancreatic enzyme replacement allow more normal growth. Pulmonary management with improved bronchodilator therapy, bronchial drainage with chest physiotherapy, and major advances in anti-Pseudomonas drugs and synergistic combinations of aminoglycoside and semisynthetic penicillin derivatives and aerosolized antibiotics have improved outcome.

Hazard Avoidance: Heat stroke and heat prostration are common with fever or hot weather.

Genetic Counseling: Prenatal diagnosis possible in most families with a living affected proband; no carrier screening of general population. Primary benefit of newborn screening is prevention of malnutrition. Families should be counseled so they can plan appropriately.

SCREENING TEST CHARACTERISTICS

Type of Test: Immunoreactive trypsin (IRT) test of blood spots is screening test in neonatal period. There is a sharp decline in plasma concentration during first 6 months of life and in older children declines.

Cost: $1 screening test (IRT).

Stability of Specimen: Dry specimen for IRT test during neonatal period. Long-term stability and optimal storage conditions not yet reported.

Field Testing: In Colorado, >100,000 newborns screened. Incidence of CF was 1:3,963.

Confirmation: Sweat test.

Accuracy of Screening Test

Sensitivity: Increased false-negative test results among those with meconium ileus. False negatives 3.8%.

Specificity: Elevated IRT result in neonatal period should have high degree of specificity because pancreatitis is extremely rare in the newborn; false-positive rate is 0.2%; ratio of true-positive to false-positive result is 1/6.

SYSTEM CHARACTERISTICS

Timing: Neonatal period; exact timing is not critical.

Coordination: Convenient to carry out in same laboratory that screens for phenylketonuria and hypothyroidism.

Follow-up: Specialized CF clinics already operational.

Public Awareness/Education: Provided at time of infant’s birth; little general awareness.

Physician Awareness/Acceptance: Provided by state programs, regulations, and/or law.
ONGOING STUDIES: Pilot studies in Colorado and Wisconsin. Wisconsin study is ongoing; this is a blind study of the benefits of early identification. Extensive research is needed to determine value of early treatment, reliability, and validity of screening methods and benefits and/or risks of early detection.

RESEARCH VALUE OF SCREENING: Impact of presymptomatic diagnosis on child and on reproductive planning and family ecology unknown. Value of IRT test in decreasing number of missed CF cases unknown. Research enhanced by identification of large population of presymptomatic patients.

HAZARDS AND/OR PROBLEMS RELATED TO SCREENING: There is concern that children with false-positive IRT test results and those with accurate diagnosis may suffer psychologic damage. Physicians may dismiss consideration of CF based on normal screening results and then may not respond appropriately to symptomatic patients. Litigation may result from false-negative results. Perhaps educational brochures given to patients should include the current false-negative rate.

RECOMMENDED READING

DUCHEENNE MUSCULAR DYSTROPHY (DMD)

Progressive deterioration of muscles beginning in infancy and leading to death in second or third decade. Inheritance is X-linked recessive.

DISEASE CHARACTERISTICS

Incidence: 1:3,000 to 1:5,000 male live births; 1:11,500 overall (boys and girls).

Racial/Ethnic Variability: Probably independent of ethnic background.

Sex Ratio: X-linked inheritance. With few exceptions, only boys are affected.

Severity/Variability Without Screening

Mortality: There is no medical treatment for DMD. Patients with DMD die between ages 18 and 25 years. Patients with Becker muscular dystrophy survive longer.

Developmental Disabilities: Delayed overall development in 10% to 30%. Mean IQ is about 80.

Physical Disabilities: No clinical signs at 0 to 2 years; 2 to 6 years slight muscle weakness; 3 to 7 years is usual age for diagnosis; 6 to 9 years increasing muscle weakness and contractures; 9 to 15 years walking with leg braces or use of wheelchair; >15 years completely dependent on help; 18 to 25 years death due to heart and lung complications.

Potential for Symptomatic Diagnosis: Diagnosis between 3 and 7 years of age for 70% of patients. Specialist may make diagnosis earlier, especially in families with previously affected children.

Variability: Progression rate variable but early death (second or third decade) is rule. Becker muscular dystrophy (an allelic form) is a similar but more slowly progressive disorder with longer survival.

With Screening and Treatment: No definitive medical treatment available. Physical therapy and bracing may prolong function and ambulation.

Mortality: Not changed.

Developmental Disability: Probably not changed.

Physical Disability: Early diagnosis leads to early physical therapy which may delay onset of physical disability. No effect is yet proved for beneficial influence on later physical development.

Variability: No change.

Possible Interventions

Treatment: No definitive treatment available.

Hazard Avoidance: None. Early diagnosis may allow family to make life-style decisions with consideration of child's progressive disability. Prolonged immobilization should be avoided. General anesthesia may lead to malignant hyperthermia.

Genetic Counseling: X-linked recessive inheritance. One third of cases are due to new mutations. Estimates predating DNA era have suggested that as many as 35% of cases are preventable by counseling and testing female relatives, but only 8.4% of second cases can be prevented in two-children families. New DNA analyses for detection of female carriers and prenatal diagnosis may increase prevention rate. Without screening and presymptomatic diagnosis, many families will have additional children without opportunity for prenatal diagnosis.

Other Advantages: Early diagnosis helps families
to make practical decisions about life with a handicapped child and to avoid prolonged “diagnostic odysseys.” DNA analyses may reduce anxiety for individuals shown to be carriers or individuals most probably unaffected.

SCREENING TEST CHARACTERISTICS AND CONFIRMATION

Type of Tests: Determination of creatine kinase (CK) in dry blood spots by either fluorescence or kinetic bioluminescence test.

Cost: Reagent costs approximately $0.75 test. Total costs including obtaining blood sample and complete organization of a voluntary freestanding screening program costs approximately $10 per baby tested. Coordination with existing newborn screening would result in costs similar to other metabolic disorders.

Stability of Specimen: CK activity in dry blood spots decreases about 25%/wk at room temperature and normal humidity. Can be stored frozen (with desiccant) for at least 1 month.

Field Testing: In voluntary program in West Germany, parents and pediatricians are provided with test envelopes containing information brochures and test cards. Tests are performed between 4 weeks and 1 year of age. Approximately 15% of male infants are screened. Pilot programs in France (Lyon) and Canada (Manitoba) test newborns.

Confirmation: Increased CK activities must be confirmed by conventional CK tests on serum. DMD must be diagnosed by other enzyme tests (SGOT, SGPT, lactic dehydrogenase, aldolase), electromyography, histologic analysis of muscle biopsy material, and family history.

Accuracy of Screening Test

Sensitivity: Bioluminescence assay. No false-negative tests for DMD are known.

Specificity: 0.9998. False-positive rate is 0.019% (>300 U/L). Test also detects other diseases with increased CK activities, such as Becker muscular dystrophy, limb girdle muscular dystrophy, CK-BB blood anomaly.

SYSTEM CHARACTERISTICS

Timing: Controversial. Testing at 4 weeks of age decreases false-positive rate, because normal newborns may have elevation of CK levels.

Coordination: Voluntary screening program in West Germany in cooperation with German Muscular Dystrophy Association. Would not be easily incorporated into existing neonatal screen but might be done on second specimen at 4 weeks.

Follow-up: By test laboratory in cooperation with specialists for neuromuscular diseases and Muscular Dystrophy Association. Multidisciplinary muscle disease clinics are already in existence.

Public Awareness/Education: Awareness of the disorder is high. In the West German programs, information brochures are distributed in about 40% of hospitals. Television has been used to increase awareness. The possibility of screening is not widely appreciated.

Physician Awareness/Acceptance: Few physicians know that newborn screening is possible.

ONGOING STUDIES: DNA analyses will be added to West German screening program to improve genetic counseling of affected families.

RESEARCH VALUE OF SCREENING: Epidemiology of DMD. Screening for young DMD carrier girls may become feasible.

HAZARDS AND/OR PROBLEMS RELATED TO SCREENING: No physical hazard. Whether psychologic problems are created by early diagnosis of DMD is debated but improbable.

RECOMMENDED READING


GALACTOSEMIA

Inherited disorder of galactose metabolism leading to failure to thrive, vomiting, liver disease, cataracts, and mental retardation in untreated survivors. Lethal in most cases.

DISEASE CHARACTERISTICS

Incidence: 1:60,000 to 1:80,000.

Racial/Ethnic Variability: Not known.

Sex Ratio: M = F.

Severity/Variability Without Screening

Mortality: Usually fatal.

Developmental Disabilities: Present in survivors.

Physical Disabilities: Cerebral palsy, ataxia, seizures, mental retardation, cataracts, and liver disease.
Potential for Symptomatic Diagnosis: Fair.

Variability: Duarte/galactosemic compound heterozygote may be ascertained by newborn screening and may be confused with classical galactosemia. Heterogeneity is present in transferase enzyme with many different variants.

**With Screening and Treatment**

Mortality: None expected but some infants may die before the results of the screening test are available because of susceptibility to *Escherichia coli* septicemia.

Developmental disabilities: Mean IQ in normal range, but range is wide. Visual-perceptual and other learning disabilities are common.

Physical disabilities: None in childhood but ovarian failure with hypergonadotropic hypogonadism and primary or secondary amenorrhea has occurred in many treated girls.

Variability: Genotype classification necessary to determine treatment and compare outcomes.

**Possible Interventions**

Treatment: Galactose-free diet begun as soon as possible and continued throughout life. Monitoring of galactose-1-phosphate levels determines compliance. Evaluation for learning disabilities should be performed as needed and appropriate intervention arranged.

Hazard avoidance: Lactose, especially in dairy products and breast milk. Lactose is a disaccharide. Galactose, a product of lactose metabolism, is the compound that these persons cannot metabolize.

Genetic counseling: Autosomal recessive. Couples at risk have 25% recurrence risk in each pregnancy. Prenatal diagnosis is possible.

**SCREENING TEST CHARACTERISTICS**

**Type of Test:** Test for elevated blood galactose content: microbiologic test using *E coli* or *E coli* in combination with a bacteriophage (Paigen test). Test for deficient enzyme activity: fluorescent spot-screening test (Beutler test).

**Cost:** $0.50 per test.

**Stability of Specimen:** Satisfactory for screening, but stability of transferase drops in hot, humid climates and false-positive results become common.

**Field Testing:** Complete in numerous states.

**Confirmation:** Quantitative measurement for galactose, galactose-1-phosphate, and starch gel electrophoresis for transferase enzyme. Family studies may be necessary to determine the genotype.

**Accuracy of Screening Test**

Sensitivity: Excellent for classical transferase deficiency, but partial deficiencies (especially Duarte/classical galactosemia or Duarte/galactosemic compound heterozygotes) may be missed.

Specificity: Varies with test. False-positive results especially high during hot summer months with Beutler test.

**SYSTEM CHARACTERISTICS**

**Timing:** Screening by measurement of enzyme galactose-1-phosphate uridyl transferase accurate at any time. Methods measuring galactose accumulation require ingestion of milk. Patients who have had transfusions may have negative Beutler test findings for as many as 2 to 3 months. Rapid screening is necessary because of *E coli* sepsis and presence of neurologic residua in patients treated late.

**Coordination:** Commonly provided through state departments of health in association with other neonatal metabolic screening.

**Follow-up:** Specialized metabolic/genetics clinics providing nutritional, psychologic, nursing, biochemical, and pediatric care.

**Public Awareness/Education:** Usually provided during neonatal period; public generally unaware.

**Physician Awareness/Acceptance:** Provided by state programs, regulation, and/or state law.

**ONGOING STUDIES:** Sterility in girls, speech problems and learning disabilities in treated patients, rigidity of diet restrictions, clinical manifestations of compound heterozygotes and other variants.

**RESEARCH VALUE OF SCREENING:** Low at this time.

**HAZARDS OF SCREENING:** None apparent.

**RECOMMENDED READING**


HOMOCYSTINURIA

Autosomal recessive disorder in pathway for breakdown of methionine. Most common cause of homocystinuria is a block in enzyme, cystathionine synthase. Elevated levels of homocysteine, methionine, and metabolites of homocysteine accumulate in blood and urine of these patients. Clinical problems include thromboembolism, ectopia lentis, osteoporosis, mental retardation, seizures, psychiatric disturbances, and myopathy.

DISEASE CHARACTERISTICS

Incidence: 1/50,000 to 1/150,000.

Racial/Ethnic Variability: United States ≤1/200,000 ascertained by screening; Ireland, Australia, and Great Britain 1/82,000.

Sex Ratio: M = F.

Severity/Variability Without Screening

Mortality: Death reported <1 year of age. Approximately 50% of untreated individuals die by 25 years of age; death is frequently due to thromboembolic events.

Developmental Disabilities: Developmental delay is reported in 65% to 80% of untreated individuals.

Physical Disabilities: Include marfanoid habitus, ectopia lentis, glaucoma, cataracts, osteoporosis with bone deformities, high palatal arch, and muscle weakness with shuffling gait. Arterial or venous thromboses may involve cerebral, pulmonary, renal, and myocardial circulation.

Potential for Symptomatic Diagnosis: Potential for early clinical diagnosis is limited. Ocular abnormalities may lead to diagnosis as may other medical complications. However, nonspecific features may not lead to definitive test, which is measurement of serum and/or urine amino acids.

Variability: Extremely variable disorder clinically, ranging from benign to severe early findings. Other metabolic forms of homocystinuria are vitamin B₁₂ metabolic abnormalities and 5,10-methylene-tetrahydrofolate reductase deficiency. Not all affected individuals have elevated methionine levels. Severe vitamin B₁₂ deficiency may lead to homocystinuria and methylmalonic acidemia.

With Screening and Treatment

Mortality: Treatment appears to reduce risk of thromboembolic episodes.

Development disabilities: It appears that mental retardation is prevented.

Physical disabilities: Ectopia lentis appears to be delayed, and incidence of convulsions is reduced.

Variability: Clinical variability remains even with therapy. However, the relationship between this variability and underlying metabolic problem or compliance are yet to be ascertained.

Possible Interventions:

Treatment: Depends on underlying cause of homocystinuria. Approximately 50% to 80% will not respond to vitamin B₆. Nonresponsive patients with cystathionine synthase deficiency should be treated with a methionine-restricted, cystine-supplemented diet. Betaine may also be helpful. Pyridoxine responsiveness should be ascertained. When patients have methylmalonic acidemic and homocystinuria, vitamin B₁₂ treatment may be beneficial. Aspirin and dipyridamole have also been used to prevent thromboembolic phenomena.

Hazard Avoidance: Dietary methionine. Patient with one thromboembolic episode is at high risk for subsequent episodes, and treatment should be managed aggressively. Surgery may increase risk of thromboembolism, but data indicate that most surgery can be managed with relative safety.

Genetic Counseling: Specific entity must be ascertained, but all are autosomal recessive. Prenatal diagnosis is available.

TEST CHARACTERISTICS

Type of Test: Bacterial inhibition assay (BIA) to determine elevated level of blood methionine. Methionine elevation may be delayed, especially in vitamin B₆-responsive patients, many of whom may be missed with screening at time of nursery discharge.

Cost: When added to existing screening program with other BIA testing, $0.50

Stability of Specimen: Unknown.

Field testing: Still in progress to determine frequency of disease, ethnic variability, efficacy of screening, and therapy.

Confirmation: Quantitative amino acids to measure methionine and homocysteine.

Accuracy of Screening Test

Sensitivity: Limited information.

Specificity: High; >99.9% depending on individual program.
SYSTEM CHARACTERISTICS

Timing: Significant proportion of patients are missed using specimen obtained in first three days of life, because methionine level has not risen sufficiently; this probably accounts for difference in screening frequencies between United States and United Kingdom; screening specimens are obtained at five to seven days in United Kingdom.

Coordination: May be incorporated into existing programs, but use of initial specimen leads to missed cases.

Follow-up: Specialized care necessary including ability to monitor amino acids and provide nutritional assessment and planning.

Public Awareness/Education: Poor.

Physician Awareness/Acceptance: Awareness limited, and even with increased awareness, it is difficult to make early clinical diagnosis. However, the diagnosis should be considered in individuals with characteristic eye problems and early thromboembolic episodes.

ONGOING STUDIES: Programs continue to evaluate efficacy of screening and early treatment.

RESEARCH VALUE OF SCREENING: High. Efficacy of early diagnosis and treatment remains significant issue. Improvement in screening to decrease numbers of missed patients is also important. Optimal treatment regimens still under investigation.

HAZARDS AND/OR PROBLEMS RELATED TO SCREENING: Overuse of vitamin B$_6$ can cause neuropathy.

RECOMMENDED READING


DISEASE CHARACTERISTICS

Incidence: 1:10,000 to 1:25,000 (United States).

Racial/Ethnic Variability: Considerable. White: 1/6,000 Ireland, 1/8,000 to 10,000 W. Germany; Black: (less common than white); Asian: 1:60,000 (Japan), 1:20,000 (China).

Sex Ratio: M = F.

Severity/Variability Without Screening

Mortality: Classical PKU is not lethal, but data concerning institutionalized patients showed that life span was reduced. Cofactor variants may lead to death in childhood.

Developmental Disabilities: In 95%, IQ <50. Some milder forms of hyperphenylalaninemia do not reduce intelligence.

Physical Disabilities: Convulsions, hyperactivity, and eczema common.

Potential for Symptomatic Diagnosis: In symptomatic patients, disease is rarely diagnosed before 6 months and usually only after mental retardation is obvious. Some cases are not diagnosed until subsequent sibling ascertained by newborn screening.

Variability: Milder forms of hyperphenylalaninemia occur. Cofactor deficient variants may cause progressive neurologic deficits ultimately leading to death; these patients require special testing to identify defect in biotin metabolism so that appropriate therapy can be initiated. All patients with confirmed hyperphenylalaninemia should be tested to rule out biotin defects.

With Screening Diagnosis and Treatment

Mortality: No excess expected.


Physical Disability: None with treatment.

Variability: Cofactor related to causes of hyperphenylalaninemia may need other treatment and have poorer prognosis. Hyperphenylalaninemia may not require treatment if serum phenylalanine concentration remains <10 to 15 mg/dL.

Possible Interventions

Treatment: Dietary restriction of phenylalanine with regular monitoring of serum phenylalanine levels. This is highly effective when begun earlier than 4 weeks (optimally as soon as possible) and should be continued indefinitely. Treatment of adults is generally recommended especially for

PHENYLKETONURIA (PKU)

Autosomal recessive aminoacidopathy leading to mental retardation when untreated. Most cases are result of phenylalanine hydroxylase deficiency but some are due to biotin deficiency.

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Autosomal recessive aminoacidopathy leading to mental retardation when untreated. Most cases are result of phenylalanine hydroxylase deficiency but some are due to biotin cofactor deficiencies.
women of childbearing age. Treatment after CNS damage has been sustained will not reverse retardation but may lead to some improvement in behavior control. Treatment requires special formula and use of low-protein foods. A nutritionist and specially trained physician are necessary to coordinate therapy. Formula, low-protein foods, and laboratory monitoring are moderately costly. Compliance is a problem for many adolescents.

Hazard Avoidance: Aspartame (NutraSweet, Equal); high-protein foods.

Genetic Counseling: Autosomal recessive. Prenatal diagnosis and carrier testing are available by DNA analysis. Infants of untreated affected mothers (“maternal PKU”) may have microcephaly, retardation, and congenital heart disease even when not affected by PKU. Efficacy of treatment, to prevent fetal effects, is under study; preliminary data show treatment beginning prior to conception and continuing throughout pregnancy could be beneficial.

SCREENING CHARACTERISTICS AND CONFIRMATION


Cost: $1.25 per test.

Stability of Specimen: Short-term excellent. Excellent when frozen at −70°C. Stability under ambient conditions for several years is unknown.

Field Testing: Complete.

Confirmation: Quantitative measurement of serum phenylalanine, tyrosine, urinary pteridines, and blood dihydropteridine reductase (to exclude cofactor variants). Quantitative phenylalanine and tyrosine are available in many laboratories; pterin measurements are available in a few centralized laboratories.

Accuracy of screening test

Sensitivity: Dependent upon age at testing and cutoff used. At less than 24 hours of age and 4 mg cutoff, 16% will be missed; at 24 to 48 hours of age, 2.2% will be missed.

Specificity: 99.9%

SYSTEM CHARACTERISTICS

Timing: Newborn >24 hours of age and before seven days. Rescreening at 2 to 4 weeks may not be cost effective. Infants screened before 24 hours of life should be rescreened. All infants should be screened at time of nursery discharge or transfer regardless of age. Sick infants and premature infants should be screened by seven days of age, regardless of feeding history or antibiotic treatment.

Coordination: Commonly provided by state departments of health.

Follow-up: Usually in specialized clinics (state or regional) which are already established. There is, however, a lack of adequate public and third-party support for costs of treatment. Registries of affected girls and women are being developed to track those at risk for maternal PKU.

Public Awareness/Education: Commonly provided at time of infant’s birth. Brochures for parents may be available before or after delivery.

Physician Awareness/Acceptance: Provided by state programs, regulations, and/or law. Routine mandated screening may lead to less efficient diagnosis of missed, symptomatic persons.


RESEARCH VALUE OF SCREENING: Low at this time. DNA analysis from dried blood spots is under study.

HAZARDS AND/OR PROBLEMS RELATED TO SCREENING: Maternal PKU may become more common, with resultant damaged infants. Continuing treatment into adulthood may result in subtle dietary deficiencies, especially of trace minerals. Missed patients may include those not born in hospitals, those born in countries other than the United States, and those born prior to routine screening.

RECOMMENDED READING


SICKLE CELL DISEASES

SS, SC, and Sβ-THALASSEMIA

Autosomal recessive disorders resulting from synthesis of abnormal β-chains of hemoglobin. Affected individuals may have overwhelming sepsis,
chronic hemolytic anemia, episodic vascular occlusive crises, hyposplenism, periodic splenic sequestration, and bone marrow aplasia. Some other hemoglobinopathies may also be detected by sickle cell screening.

**DISEASE CHARACTERISTICS**

**Incidence:** 1:400 (US blacks). Overall incidence depends upon ethnic distribution in target population.

**Racial/Ethnic Variability:** Common in blacks; less severe forms common in Arabs, East Indians, and those of Middle Eastern and Southern European descent.

**Sex Ratio:** M = F.

**Severity/Variability Without Screening**

Mortality: Can be lethal especially in early infancy or childhood. All probably have reduced lifespan, but survival into adulthood is common.

Developmental Disabilities: Usually none. Cerebral vascular accidents or sequelae of meningitis may lead to neurologic deficits. In school-aged children, there may be frequent absenteeism.

Physical Disabilities: Aseptic necrosis of bones, leg ulcers, neoproliferative retinopathy, serious infections, cerebral thromboses, renal concentrating defects, and delayed maturation.

Potential for Symptomatic Diagnosis: Clinical diagnosis rarely made until approximately 1 year of age. Overwhelming sepsis may occur prior to any other symptoms.

Variability: Marked clinical variability (from asymptomatic to death in early life). Various combinations of β-chain mutations (SS, SC, S-thal, etc). Clinical severity is also influenced by the presence of other mutations, eg, thalassemia.

**With Screening, Diagnosis, and Treatment**

Mortality: Early death from overwhelming sepsis may be prevented by heightened vigilance, penicillin prophylaxis, and immunizations. Death from acute splenic sequestration and aplastic crisis may be prevented/reduced.

Developmental Disabilities: Risks lowered by aggressive treatment of infection and dehydration. Remedial schooling as needed for acquired disability.

Physical Disabilities: Unclear whether improved by blood transfusions, prevention and treatment of dehydration and acidosis, use of pneumococcal vaccine, aggressive antibiotic treatment for infections, judicious use of oxygen, and parent and patient education.

Variability: With screening and penicillin prophylaxis, risks of sepsis and death in infancy can be significantly decreased.

**Possible Interventions**

Treatment: See above. Prophylactic antibiotics. Immunization against pneumococcal and *Haemophilus influenzae* infection. Rapid access to appropriate medical care.

Hazard Avoidance: Low atmospheric oxygen (high altitudes), dehydration, cold exposure, excessive exertion, and possibly emotional stress.

Genetic Counseling: Autosomal recessive. Carrier testing available by hemoglobin electrophoresis or DNA studies. Prenatal diagnosis is available by DNA analysis.

**SCREENING CHARACTERISTICS AND CONFIRMATION**

**Type of Test:** Hemoglobin electrophoresis on cellulose acetate, followed by citrate agar, isoelectric focusing, and/or high-pressure liquid chromatography on cord blood or dried heel stick blood spot.

**Cost:** $1.50 per test.

**Stability of Specimen:** Filter paper specimens or cord blood is stable for as many as several weeks frozen.

**Field Testing:** Numerous screening programs are currently in place. Locating all infants with positive test results has been a problem in some areas. Must decide how to deal with carrier infants.

**Confirmation:** Hemoglobin electrophoresis and parental testing.

**Accuracy of Screening Test**

**Sensitivity:** Unknown. New York state program has no known missed cases.

**Specificity:** Dependent upon type of test used. New York state found 0.04% needed follow-up test; 97.9% of positive results were confirmed.

**SYSTEM CHARACTERISTICS**

**Timing:** Cord blood or heel stick blood at any time following birth.

**Coordination:** Central coordination needed; can be coordinated with other neonatal tests. Local sickle cell organizations may be important resource.

**Follow-up:** Coordinated comprehensive care by specialized clinics (state or regional needed); some private primary care practitioners.

**Physician Awareness/Acceptance:** Highly variable: poor to good.
Public Awareness/Education: Provided by local sickle cell organizations. Many popular misconceptions.

ONGOING STUDIES: Prospective studies regarding impact of early diagnosis and vigorous treatment on prognosis; methods of treatment to prevent sickle crises; optimal use of blood products, oxygen, and vaccines.

RESEARCH VALUE OF SCREENING: Encourage research concerning treatment. Natural history studies. Determine whether carrier counseling is valuable for (1) future pregnancies and (2) subsequent generations. Research concerning new methods for screening including immunologic approaches and DNA analyses; these may be applicable to other disorders.

HAZARDS AND/OR CONCERNS RELATED TO SCREENING: Stigmatization. Confusion about meaning of being a carrier; concerns about confidentiality; identification of nonpaternity; discrimination in work place, insurance; counseling large number of carriers.

RECOMMENDED READING
NIH Consensus Development Conference Statement Newborn screening for sickle cell disease and other hemoglobinopathies. Vol. 6(9), April 6–8, 1987

ACKNOWLEDGMENT
We thank all of the individuals who have assisted us in collecting this information.

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Newborn Screening Fact Sheets

Pediatrics 1989;83;449

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