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U.S. Newborn Screening System Guidelines: Statement of the Council of Regional Networks for Genetic Services

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The Council of Regional Networks for Genetic Services (CORN) was created in. 1985 to provide a forum for information exchange among groups concerned with public health aspects of genetic services. The newborn screening committee includes. representatives from each genetic region of the United States (equally divided among laboratories and administrators) and liaison members from related professional groups. State and, regional newborn screening programs across the U.S. vary widely in most aspects of their organization and hence their program outcome. The Newborn Screening Committee of CORN. has identified eight specific areas of mutual importance to all programs. These areas include: organization and administration; selection and evaluation of disorders for screening; communication; quality assurance; funding; diagnosis, management, treatment and counseling; program evaluation; and liability. Basic guidelines have been developed in these areas so that U.S. screening programs may begin to achieve uniform consistency in outcome. The guidelines are not intended to judge standard of care, but rather are meant as a framework about which to mold newborn screening programs.

Key words: Newborn; Screening;. Guidelines; CORN

Background

The Council of Regional Networks for Genetic Services (CORN) is a federally funded project to improve the quantity, quality, and availability of cost effective

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genetic services in the United States. CORN was developed in 1985 in response to the need for an organization both to coordinate activities among federally funded genetic service networks encompassing the entire U.S. and to implement programs of national significance that emerge from regional initiatives in such priority areas as quality assurance, data collection and education. Two delegates from each network serve on the CORN steering committee with additional representation from the Alliance for Genetic Support Groups, national sickle cell disease programs and other organizations involved in genetic services. CORN members comprise a unique organization of genetic service providers, public health personnel and consumers. The organization maintains a strong focus on the public health components of genetic services in its goals and activities.

The Newborn Screening Committee of CORN was formed in 1987, to address newborn screening issues of regional and national concern regarding program implementation and facilitation. Members of this committee have served as expert reviewers on a federally sponsored panel assisting state newborn screening programs in self evaluation as an aid to improvement of service delivery. Observation of similar structural and functional problems among the state programs surveyed, coupled with a CORN initiative (assistance to local screening efforts through general administrative guidelines to increase national screening. uniformity and effectiveness), led to development of these guidelines. They are the result of over three years of committee deliberations and their continual review and update is intended to provide meaningful guidance to local newborn screening efforts both now and in the future. While this information may prove useful to newborn screening programs in other countries, these guidelines were developed for utilization only in the U.S. and consideration to geographic, political, and economic influences elsewhere were not a factor.

Introduction

Newborn screening is an essential preventive ~ public health program for early identification of disorders that can lead to potentially catastrophic health problems. Its efficient and productive outcome is governed by the smooth integration of specimen collection, laboratory analysis, follow-up contact and effective treatment.

The following basic program guidelines have been developed by the Newborn Screening Committee of the Council of Regional Networks for Genetic Services (CORN) so that screening programs across the United States may begin to achieve uniform consistency in outcome. Committee members recognize that geographic, political and economic factors affect the manner in which newborn screening programs function; however, guidelines considered both essential and achievable by a national, broad-based committee of professionals in this field should provide a basis on which to pattern a successful system. These guidelines should not be misused to judge standard of care, but rather should be used as a framework about which to mold the screening program.

From the outset, we must recognize that newborn screening is a system that

includes private medical practitioners, laboratory personnel, administrative follow-up personnel, tertiary care centers, third-party payers, and others with the same ultimate goal. This system must be designed to function smoothly and efficiently within the governmental/political framework which gives it life.

1.0. Organization and administration

1.1. Legislation

Where legislation is in place, it is preferable to authorize mandatory screening so that program changes may be made through board of health or other administrative action, without new legislation. Rules and regulations establishing responsibility for proper timing of specimen collection, specimen submission, record keeping, laboratory analysis, follow-up, and treatment should outline how the enabling legislation will be implemented. Although several states have no legislation requiring screening (voluntary programs appear to be reaching a high percentage of the desired population in these states), occasional system difficulties, such as financing problems, might be avoided if a legislative mandate for neonatal screening were in place. Some state programs have legislation specifically defining the intent of the program and the disorders that are included. In these programs, it may be extremely difficult to add or delete screening disorders. Responsibility for program details, therefore, should reside outside of the primary enabling statute.

1.2. Scope of responsibility

Documentation of the beginning and ending of organizational and individual responsibilities for medical, laboratory, and follow-up personnel must be clearly established and followed. Realistic, functioning procedural manuals for each of the responsible parties should be developed and combined into an overall newborn screening system manual. The procedures and protocols developed should be used in actual practice by those responsible. Whereas an ideal system may serve as a goal towards which protocols may be oriented, system manuals should define minimum standards and reflect actual practice, serving as usable reference sources that clearly define each step of responsibility. Starting and ending points of each function must be indicated so that smooth integration of system services is easily accomplished.

1.3. Advisory committees

The use of at least one advisory committee, including outside professional and consumer representation, is encouraged. Such committees) may be used to solicit administrative and other program advice as well as external advocacy. Involvement of persons independent of the responsible governmental body enhances the credibility of the program. This committee may be a subcommittee of a larger genetics advisory group, if appropriate, and should involve persons with suitable backgrounds and

interests to offer constructive aid to the system. Such areas as scope of responsibility of system components, screening protocols, and fiscal policy, may benefit from outside advice and advocacy. This committee should not assume responsibility for internal governmental matters or for technical decisions, but rather should act as a group of consultants that helps in developing approaches, planning future directions and problem solving.

1.4. Program centralization

The newborn screening program requires a strong, centralized, administrative staff, knowledgeable in all aspects of the program and concerned with efficient, effective program implementation. Some of the follow-up tracking may be decentralized, provided a central data bank is kept updated so that no children with disorders are lost to follow-up.

Consolidation of newborn screening laboratory testing is advised. Centralization promotes economy and efficiency in performing large numbers of screening procedures. Furthermore, the rarity of most screened disorders results in infrequent observation of abnormal tests, making it preferable to perform large numbers of analyses in order for the laboratory to observe 'real' cases from time to time. It has been suggested in one source that laboratories be required to test at least 50,000 samples annually [2]. States with smaller birth rates may find it efficient to combine efforts in a regional laboratory. It may not be practical to operate within this suggested quota of specimens analyzed. -In this case, it is essential that analytical proficiency be optimized through testing blinded control specimens, exchange of specimens with other laboratories, or external proficiency testing.

2.0. Selection and evaluation of disorders for screening

The disorders included in a screening program should be logically and systematically selected [7J. Some countries have developed priority listings for disorders to be considered for screening [4]; however, such rankings have not yet occurred in the United States. All U.S. programs currently perform screening for phenylketonuria and congenital hypothyroidism. It has been recommended by a National Institutes of Health (NIH) consensus panel, that newborn screening for sickle cell disease be mandated by all programs [4]. Thus, there is increased emphasis on sickle screening and approximately 80°/a of all U.S. programs include this testing.

2.1. Addition and deletion of disorders

To ensure that decisions to add or delete screening tests (see Sec. 1.1) are intelligent, and informed, demography (including genetic composition), methodology, outcome, and economics must be considered. Cost-effective, efficient screening should produce the desired effect on. infant morbidity and mortality through a well designed pilot program and the experience of others. Before any screening disorders are added or

deleted, sufficient information should be gathered to support the changes. Specifically, incidence data and population statistics must indicate that screening for the disorder will result in detection of a reasonable number of cases. Additionally, the laboratory protocol proposed must be sufficiently sensitive to serve as a viable method for use with the specimens of interest. These specimens must be economically and technically feasible to collect, transport and analyze. Screening should be initiated only if effective intervention is accessible to all affected individuals.

2.2. Laboratory methods

Analytical methods should be of sufficient sensitivity and specificity, with adequate quality control, to ensure maximum disease detection with minimal false negative. results. Low false positive rates are necessary to prevent overburdening of the follow-up system. Laboratory services should be centralized when possible and include multistate regionalization (see Sec. 1.4). Laboratories performing screening should adhere to professional guidelines in common usage by the College of American Pathologists (or other suitable accrediting body) concerning the type and frequency of use of analytical control material. Successful subscription to an external proficiency testing program is essential to demonstrating credibility of the procedures used in the screening laboratory. If no such program exists for the analyte and/or matrix involved, programs are encouraged to document reliable results on specimens exchanged with other well established laboratories in the field. Appropriate sensitivity and specificity limits are difficult to define; however, their importance cannot be overemphasized with respect to credibility and cooperation from the physician community in following up on abnormal results.

2.3. Follow-up

The newborn screening system must ensure follow-up of any positive, or potentially positive, result to the point of resolution. This is best accomplished when responsibilities and procedures for follow-up are assigned to a specific follow-up coordinator. All details of follow-up should be clearly defined. Data transfer must be timely and complete so that adequate information is available to the follow-up persons. Follow-up responsibility may reside within or outside of the laboratory; both types of follow-up are used in the United States. The beginning and ending of follow-up, along with organizational and individual responsibilities, must be clearly defined. These will usually include all activity from the time of notification of an abnormal result until the time the patient receives treatment. Initial notification to physicians that patients have medically significant abnormal results should be by telephone, if possible. A confirmatory letter should then be sent clearly outlining subsequent follow-up steps through case resolution. A successful follow-up protocol must include procedures for reaching a conclusion for each case, even if that conclusion is “lost to follow-up”.

2.4. Repeat tests

Repeat testing should be performed whenever the first test result's reliability is questioned. Linkage of second test results to the initial screening specimen is important as a means of controlling quality and completing follow-up information. When transfusions or antibiotic treatment have been given before the appropriate laboratory specimen is collected, a mechanism for repeat testing should also exist. The physician or other person attending the newborn should be responsible for the timing and redrawing of repeat specimens; however, notification of the need for retesting is a program responsibility.

Routine second testing of all or selected newborns should be considered on the basis of resources available and cost effectiveness. To avoid biological false negative results in the early newborn period, a second specimen can be obtained later. The full benefit of detecting late onset disorders has not been measured.

3.0. Communication

Rapid, effective communication of abnormal results is essential and should include transmission of critical information, by telephone, at the earliest opportunity. Proper documentation is also necessary, given the medical-legal environment in which. screening must function.

3.1. Documentation

Documentation of specimen collection (or refusal), laboratory analysis (including quality control), result reporting, and physician and patient contact are essential. Such documentation must withstand legal scrutiny and must be maintained until the legal statute of limitations expires. Many states operate under. the concept of 'informed dissent' whereby documentation is necessary only if the screening service is refused by the patient. In these programs, the legislation or rules (regulations) governing screening require that all infants be screened except in specific instances such as religious conflict.

The person submitting the specimen should document the collection and transmittal of the specimen, and the laboratory should document its receipt and analysis. Receipt of results on each patient tested is proof that specimen transmittal has occurred. Programs must ensure rapid and direct communication of results from the laboratory to the persons responsible for the patient in all cases, regardless of the results - normal, abnormal or unsatisfactory. If abnormal results are obtained in the laboratory, proper transfer of these results to the follow-up coordinator must be documented. Likewise, transmittal from the follow-up coordinator to the person responsible for the infant's care must also be documented. Practitioners are responsible for documenting communications with the patients. Such documentation may include any of a number of forms such as paper or computer storage medium. Program officials should consult legal counsel for specific advice.

3.2. Computers

Computerization of the newborn screening program is cost-effective and provides better system control. Since the entire newborn screening system must be monitored by program administrators, computerization can provide a valuable management tool. Justifications for computerization include more efficient public service, through time savings, improved accuracy, and more extensive data assessment for program evaluation and improvement.

Proper design of the computer system's hardware and software can improve program efficiency and expand its scope. Computerized screening programs should strive to include on-site demographic data collection and submission, laboratory data management and reporting, follow-up result reporting and data collection, and analysis and program documentation. Programs should not expend unnecessary effort in developing elaborate systems without first surveying commercial and public newborn screening systems that have already been implemented. Some public programs are available at little or no charge to other newborn screening systems.

With careful thought and planning, program officials can develop a computer system that improves many aspects of the screening program. Developing computer systems that actually decrease program personnel is quite difficult; however, the available staff is often more efficiently utilized to accomplish expanded or multiple tasks within equivalent time periods. Ideally, the computerized newborn screening system includes demographic transmittal from the point of collection to the laboratory, data management within the laboratory, result reporting to the submitter and to the follow-up coordinator, generation of follow-up communications, documentation of all contacts on abnormal results (laboratory to follow-up, follow-up to physician, and extended follow-up), records for diagnosed patients, disease registries and linkage to birth records.

3.3. Education

Public awareness coupled wish professional and patient education are significant program responsibilities that must be part of the complete screening system. The importance and intent of the screening program must be properly and adequately communicated to all persons involved. Educational materials for parents should be available along with similar information for concerned professionals. Parent information .is most effective when developed on an elementary level, with appropriate ethnic and. cultural sensitivity. Professional literature should be more technical. Some programs have used manuals of protocol and responsibilities as a portion of professsional education. Sound-slide and video tape presentations have also been developed. While audio-visual aids may augment educational efforts, personal contact and demonstrations have been found to be most effective. This is particularly true in educating specimen submitters about proper collection technique. Simple flow charts of both laboratory and follow-up protocols offer handy references for all professionals participating in the system. Funding for educational expenses is often overlooked but should be included as an integral part of the overall financing system.

4.0. Quality assurance

The performance of each component of newborn screening and its contribution to the overall system must undergo quality assurance and monitoring. Criteria for adequate performance must be established for each functioning unit of the system. Ideally, a blinded specimen should be prepared and submitted to periodically check the entire system from the submission of specimens to follow-up contact.

4.1. Submitter

The submitter is responsible for assuring and documenting the quality of specimen collection and patient data. The newborn screening system must begin with a specimen of adequate quality from every newborn. The specimen submitter must ensure that there is sufficient blood uniformly distributed in each target circle on the filter paper collection form and that the specimen is collected according to program guidelines. An approved standard on collection of blood on filter paper has been set forth by the National Committee for Clinical Laboratory Standards (NCCLS) [5], and its adoption by all screening programs is recommended. Similarly the American Academy of Pediatrics (AAP) [1] has set forth guidelines concerning such issues as early discharge, and intensive care situations, which also should be incorporated into screening practice.

The demographic data accompanying each laboratory specimen must be correct and complete. Failure of the submitter to provide accurate complete data, can result in difficulties in analysis, interpretation, and follow-up. Incorrect or incomplete data can result in damage to the newborn and increased legal exposure of the submitter should diagnosis and treatment be impaired. Some programs practice demographic and specimen collection error surveillance; computers can increase efficiency and facilitate this activity. Detection of submission errors, however, should result in an educational/corrective action in order for surveillance to be of benefit.

4.2. Laboratory

Successful participation in a recognized proficiency testing (PT) program along with appropriate quality control must be practiced and documented by the analyzing laboratory. A routine PT specimen analyzed quarterly for each analyte is sufficient. With new procedures or analytes, or in response to PT misses, such testing should be performed as often as necessary in order to establish reliable performance. The laboratory must document analysis, frequency of quality assurance specimens, and appropriate use of standards (or calibrators traceable to a primary standard source). The laboratory should be able to provide adequate documentation of analytical results of unknown specimens and controls upon request. Program officials should seek legal advice about the amount of documentation needed, its length of retention, and time frame in which retrieval must occur. Laboratory protocols also must be documented and updated when procedural changes occur. Such documentation

should include a clear definition of where the laboratory's responsibility begins and ends within the screening system.

4.3. Follow-up

Regular review of documentation should be included in all newborn screening systems. Procedures to ensure complete and thorough follow-up of all positive screening findings and inadequate specimens must be in place and subject to random checks to assure proper functioning. In addition to the normal flow diagrams for follow-up activities found in most programs, a complete procedure manual must be developed to clearly indicate follow-up protocols for all combinations of abnormal laboratory results. It must define where follow-up begins, the level of activity required according to the disorder and analytical result, strategies to follow as a secondary protocol, types of documentation necessary, and how to achieve final disposition. This procedure manual must be realistic and carefully followed in order to minimize legal exposure. Some programs have found computerization and linkage to birth records (see Sec. 3.2) to be of major benefit in assisting with tracking. Cumulative listings by disorder, submitter, and region are also possible; thus, program statistics may be accurately and easily monitored and problem submitters may be identified and targeted for enhanced educational efforts.

4.4. Treatment and management

Treatment and management should lead to a partnership between the patient's primary physician, the treatment center and the newborn screening program. Many programs have found success in using specialists and consultants to assist with patient treatment and act as intermediaries with the patient's private physician. The newborn screening staff must be aware of screening outcome; therefore, data regarding treatment and management should be periodically reviewed. Only through evaluation of outcome data may program effectiveness be judged. This information may be obtained in a variety of ways, such as return mail or telephone, depending on program size.

5.0. Funding

Funding is the most difficult problem confronting newborn screening systems. Not only is there a question as to source of funds, but also there are questions related to program scope and methods of reimbursement.

5.1. Sources

Sources of funding should not necessarily be limited to state tax revenues. Federal grants, private foundations, and fees for service are viable alternatives in addition to funding through Maternal and Child Health, Women, Infant and Children (WIC),

and Crippled Children Services. Many state programs have developed a fee for services. Those unable to pay for service must be supported by the program's income from fees. In some states, financial support for all or portions of the program may be obtained from federal grants or other related programs such as WIC. In rare instances, support for particular programs has been supplemented from private sources.

All program costs should be included in any fee calculated (see Sec. 5.2). System funding should include screening laboratory analysis, follow-up services (including education), computerization, metabolic food supplements, and other treatment necessities if appropriate. Because program fees may be tied to laboratory collection kits, other funding items are sometimes overlooked. As a result, follow-up and education may be weak and fragmented. Because newborn screening encompasses many disciplines to create an efficient system, all system components must be considered in the financing structure.

5.2. Cost analysis

The societal benefits resulting from screening should be included in any cost accounting in order to fully reflect actual program benefit. A uniform method of determining program costs should be developed nationally. The recently published fiscal study prepared by the Office of Technology Assessment [6] offers some assistance.

6.0. Diagnosis, management, treatment and counseling

Diagnosis, management, treatment, .and counseling must be included as newborn screening system functions. Otherwise, there is no real purpose to screening.

6.1. Diagnosis

Screening does not equate to diagnosis; therefore, detection of some cases of disorders included in newborn screening will not occur, even in a quality program, due to biological variables and other factors. Confirmation and diagnostic follow-up must be included in a complete screening system. Clinical judgment must play an important role in the system. Testing for biopterin problems should be carried out on all patients with phenylketonuria or hyperphenylalaninemia. Similarly, hematologic examinations for clinically significant hemoglobinopathies might also be appropriate. Related procedures consistent with diagnostic follow-up of other screening disorders may be of equal importance.

6.2. Consultant resources

Pediatric subspecialists may be included as resource personnel who can act as liaisons between the governmental screening agency and the private physician. Many successful screening systems report abnormal results to the infant's physician and to consultants

specializing in the disorder of interest who are willing to offer their professional assistance. Consultants can contact the primary physician to offer assistance, if needed. This can provide an excellent feedback mechanism for the follow-up coordinator. Some state programs .use pediatric endocrinologists for hypothyroidism and congenital adrenal hyperplasia, pediatric hematologists for sickle cell disease, and metabolic subspecialists for the inborn errors of metabolism. Open communication and planning can help to alleviate problems from competition related to service areas.

6.3 Long term tracking and outcome

Long-term tracking and outcome evaluation for each screening disorder should be maintained and updated periodically. In a highly mobile society, interprogram communication is essential. Such tracking can serve as an extension of follow-up with potential benefit for long-term case management and for minimizing program losses due to relocation. Particular attention must be paid to patient confidentiality and limitations placed on data availability. As medical benefits develop for patients later in life, outcome data can provide the vital patient information necessary for tracking and health care. Benefits of this type are currently recognized for maternal hyperphenyialaninemia. Active maintenance of hyperphenytalaninemia registries (see Sec. 7.2) have assisted in locating women of childbearing age for educational follow-up. Program personnel must be advised of the latest developments with maternal hyperphenylalaninemia follow-up so that maximum benefit of this research may be realized. Cooperation with the national Maternal PKU Collaborative Study (MPKUCS) is encouraged.

6.4 Carrier counseling

Counseling programs, if appropriate, should be developed before screening in order to augment follow-up. This is particularly important in hemoglobinopathy screening. It is of primary importance that sickle cell disease be detected and treated; however, as a consequence of screening, parents and infants with sickle trait also will be identified. Because the number of carriers is extremely high relative to persons with the disease, resources for quality counseling are generally scarce. Many programs therefore, are developing liaisons with community-based sickle cell organizations in order to augment the counseling aspect of screening. All qualified, existing resources should be fully utilized to provide counseling and education to the large numbers of parents of carrier infants.

Minimum standards of professional qualification, quality assurance, and continuing education must be developed and required of all counselors. Evaluation of counseling and educational approaches should include assessment of information retention, impact on reproductive choices and cost-effectiveness.

7.0. Program evaluation

Programs should evaluate their effectiveness through documentation of the public health impact. Ongoing or periodic evaluations should be performed and monitored regularly to assess the quality of the program.

7.1. Data collection

Minimal data elements appropriate for the specimen collection form have been determined by the NCCLS j5J. Although additional data may be collected to evaluate certain program aspects, these data should be consistent with the primary objectives of the screening program. Data integrity of the newborn screening system should not be compromised by epidemiologic studies for secondary research purposes.

7.2. Outcome data

Timely, accurate reporting of outcome data should be a program priority to ensure screening effectiveness. Periodic follow-up of the status if diagnosed cases not only provides evaluation data but also allows a mechanism for patient re-entry into the medical care system, should those cases be lost. In programs where follow-up and laboratory services are decentralized, a central depository for follow-up data should be established.

8.0. Liability

Liability must be considered when planning and conducting newborn screening. It is prudent to address liability issues in making program decisions since financial losses resulting from lawsuits could have devastating effects on the screening system.

8.1. Documentation

All responsibilities within the system must be clearly defined and their completion appropriately documented (see Sec. 3.1 J. Program leaders must not assume that all tasks have been completed and all aspects of screening have been carried through without proof. Documentation must be available. The physician or hospital must be able to show evidence of a proper screen. The laboratory must record its test results along with evidence of proper standardization and control. Follow-up must be carefully documented. A contact log should be kept, listing the person contacted, date and nature of the contact, and the person making the contact. Letters sent informing physicians of the need for follow-up action preferably should be sent by certified mail. All records must be kept for a period of time in accordance with state regulations regarding medical result records for children. Program officials should consult with legal counsel on this point.

8.2. Legislation

Statutes pertaining to newborn screening within a state must be carried out. If rules and regulations are required, they should be molded for maximum program benefit. All loopholes should be closed, and all legal responsibilities carefully defined. Performing beyond the law may increase legal exposure. Programs should review the appropriate literature concerning liability issues (see entire publication in Ref. 2).

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