BIOETHICAL CONSIDERATIONS IN NEONATAL SCREENING: JAPANESE EXPERIENCES

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Abstract. Since 1979, at least 13,000 affected babies have been identified with one of the tested diseases. The outcome for patients is generally favorable if adequate treatment is given. Recently, ethical issues have arisen concerning whether or not written informed consent should be required, under what conditions the residual blood spot may be used for research purposes other than that originally designed, and whether or not the test is cost-effective. Mandatory screening seems acceptable under certain conditions, but parental education and opportunity for refusal should be part of the system. Refusal should be documented only after an attempt has been made to persuade parents to consent. Informed consent is necessary if there is uncertainty about the test's benefit to the child. Parents should be informed of the potential research value of the samples and assured that research results will not be linked to any particular/individual newborn. If identified or coded blood spots are used for research, IRB review and approval by IRB must occur. The net health care benefit from screening for six disorders in Japan was 0.25 billion yen ($2.2 million) per 100,000 screened newborns compared to $3.2 million for PKU and CH in the US for 100,000 screened newborns.

INTRODUCTION

More than 13,000 babies have been diagnosed with one of the tested diseases in the neonatal screening program in Japan. The outcome for patients has been generally favorable if adequate treatment was given early. Ethical issues have recently arisen concerning whether or not the program should be mandatory and what role consent should play in the process, whether or not residual blood spots remaining after testing should be available for research, and whether or not testing is cost-effective.

A newborn screening program should not only benefit the newborn but it should also provide support for patients' families. For implementation of the screening, bioethical considerations are of the greatest importance. According to the encyclopedia published by George Town University, bioethics is defined as "A systematic study of moral dimensions—including moral vision, dimensions, conduct, policies— of life science and methodologies". In other words, bioethics can be explained briefly as a matter of ethical, legal and social implication (Reich, 1995). Traditional sources of ethical guidelines in medicine, as described here, have a role in newborn screening (Beauchamp and Childress, 1994).

Bioethical principles in medical practice include: **respect for autonomy** of persons (respecting the individual's right to self-determination and protecting those with diminished autonomy); **beneficence** (giving highest priority to the welfare of persons and maximizing benefits to their health); **non-maleficence** (avoiding and preventing harm to persons or, at least, minimizing harm); and **justice** (treating persons with fairness and equity, and distributing the benefits and burdens of health care as fairly as possible).

ISSUES

Mandatory versus voluntary screening

Newborn screening is part of genetic testing. It is generally accepted that before genetic testing is proposed, counseling is a required and voluntary choice and written informed consent have to be obtained (autonomy) (Holtzman and Watson, 1998). As to the nature of the screening, validity and utility of the program including method and treatment should be proven in pilot studies before clinical applications are proposed (Andrews *et al*, 1994) and all screening must be of benefit to the newborn (beneficence) (Andrews *et al*, 1994). Usually parents have the right of decision concerning the health care of their offspring (parents' autonomy) (Forman and Ladd, 1995). Therefore, the parents can refuse newborn screening based on religious or cultural factors. However, there is another issue that parents should accept in newborn screening, because any proxy decision should be beneficial to the non-competent people in question (beneficence). If parents refuse the screening, their infants will lose the opportunity for correct diagnosis and effective treatment, and mental retardation could ensue (non-maleficence)

(World Health Organization, 1998). Then, should screening be on a mandatory or voluntary basis? When performed on a mandatory or voluntary basis, we will have several issues as shown here (Matsuda, 1999; Harper and Clark, 1998).

When performed on a mandatory basis: 1) all newborns will be covered in this program; 2) parents' cognition on screening is often rudimentary; 3) follow-up studies will be inadequate when the parents' permission is not given (especially in Japan); 4) parents will not have the opportunity to refuse newborn screening because of religious faith or cultural factors; and 5) disease should not be included in the program, if effective treatment or prevention of the disease is uncertain or is not available. When performed on a voluntary basis, 1) Screening will be done after a written informed consent is obtained. This is preferable because of the ethos that will be fostered in health care systems. Follow up studies will be developed easily; 2) Parents' cognition of newborn screening will be generally improved; 3) Parents' refusal for newborn screening will be accepted; 4) Disease for which treatment is uncertain, but for which an early diagnosis will aid the family could be included; and 5) It is not feasible or it is too costly to talk to parents and ask permission for screening.

Beauchamp and Childress said that, "In many clinical circumstances the weight of respect for autonomy is minimal, and the weight of non-maleficence or beneficence is maximal. Similarly in public policy, the demand of justice can easily outweigh the demands of respect for autonomy" (Beauchamp, 1994). Based on these discussions, the perception in Japan is that "neonatal screening requires voluntary consent from parents. A thorough explanation of the purpose and other information of the test must be given before consent" (Harper and Clark, 1998). Permission to do follow-up studies will also be explained since it is necessary to evaluate the screening system and the outcome. The Task Force Report of Newborn Screening in USA states that all but two states provide newborn screening on a legal mandatory basis (American Academy of Pediatrics, 2000). There are several arguments in favor of not seeking parental permission or newborn screening. First, perhaps the most important, is that screening and the potential detection in the interest of the child and the parents' objection should not hinder the screening process. The second argument is that it is not feasible or it is costly to talk to parents and ask permission. The current approach in Maryland is a simple "good will" informed consent for the total screening package which is similar to the case in Japan.

Thus, it will be concluded that for diseases preventable or treatable in the early stage, mandatory screening will be acceptable but parents should be given full information about the screening and should have the opportunity to refuse to have their newborn tested. This refusal should be documented in writing. However, it must be noted that health professionals have a duty to attempt to persuade parents to consent to having the child screened. Where there is uncertainty as to the benefits for the child being tested, screening should then not be carried out if informed consent is denied.

Screening and economics

When nationwide neonatal screening is proposed, the fund should include not only the cost of screening but also cover treatment and/or prevention. Economics and health policy analysis use two types of calculation; cost-benefit and cost-effectiveness to estimate the potentials for cost and the potentials for benefits with reduced mortality and morbidity. Cost-effectiveness analysis compares the cost of doing something to the cost of doing nothing or doing something else. In Japan, care saving per 100,000 infants was 0.25 billion yen ($2.2 million) for five diseases (Hisashige, 2000) 0.33 billion yen is needed for screening plus treatment and 0.58 billion yen will be spent, if the screening is not performed. The OTA (USA) analyses concluded that the net health care savings per 100,000 infants was $3.2 million in the case of PKU and congenital hypothyroidism (CH) (American Academy of Pediatrics, 2000). There is positive relationship between the incidence of diseases and the cost-effectiveness outcomes as shown in PKU, CH and congenital adrenal hyperplasia (Hisashige, 2000). Thus, a higher incidence has an important role in determining cost effectiveness. The goal of intervention is to save lives, prevent disability, and reduce medical expenditures. In this meaning, cost–benefit is evaluated throughout the world.

Cost-effectiveness and benefit should be established in case of newborn screening or pay–for–service system, charge to the parent, will be considered in future discussions. Also, one aspect of "benefits" of screening, such as psychological support for the family or parents, must be discussed. Social perception is another important issue for the future, for example screening for DMD, organic acidemia with unproved therapy, despite correct diagnosis being available (World Health Organization, 1998).

Use of residual blood spots for other research

The use of blood spots for research is also an issue of much discussion (World Health Organization, 1998; New York State Task Force on Life and Law, 2000). The

residual blood–spot could be used for studies, only when samples are "anonymous" or if informed consent has been specifically obtained for such purposes (Autonomy). In the guidelines of the Japan Society of Mass Screening, the conditions are as follows: 1) the purpose of the project/ research is advancement in medicine, and 2) the sample is anonymous and all identifiable characterizations are concealed (Harper and Clark, 1998). However, parents should be informed of the potential research value of the samples and should be assured that linking research results to the individual newborn will not be done. When identified or coded blood spots are used for research, review and approval of the IRB is mandatory.

CONCLUSION AND FURTHER SUGGESTIONS

The goal of newborn screening is to save lives, prevent disability, and to reduce medical expenditures. Parents should be given full information about the screening. If there is uncertainty as to benefits for the child being tested, screening should not be carried out without an informed consent. The validity and the utility of the program including the method and treatment should be proven in pilot studies even before the actual clinical application. Other aspects of a "benefit" of screening, such as the psychological benefit for the family, must be discussed. Social perception is another important issue for the future, for example screening tests for DMD or organic acidemia associated with unproven therapy, despite a correct diagnosis being available.

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