



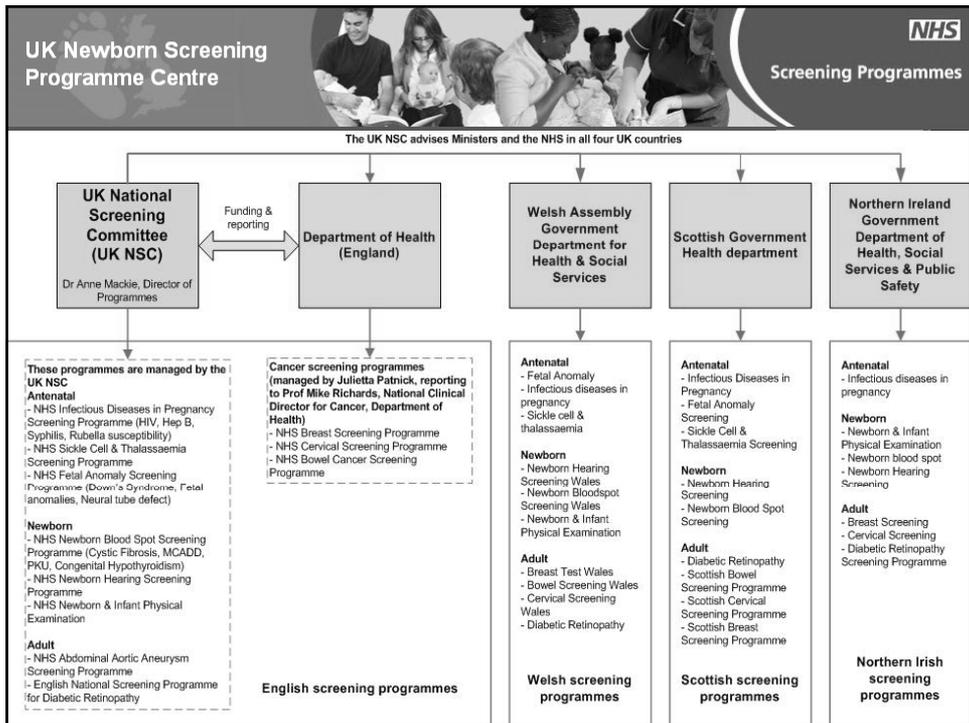
Ethical aspects of the expansion of neonatal screening program due to technological advances

David Elliman
Strategic Co-Director
UK Newborn Screening Programme
Centre



“The UK Newborn Screening Programme Centre has responsibility for developing, implementing and maintaining a high quality, uniform screening programme for all newborn babies and their parents.”

Responsible to the National Director of Screening and the Department of Health (England)



UK Newborn Screening Programme Centre  **Screening Programmes**

Current Newborn Bloodspot Screening in UK*

- Phenylketonuria – 1950s (urine); 1969 (blood)
- Congenital Hypothyroidism – 1980
- Sickle Cell - 2006
- Cystic Fibrosis - 2006/7
- MCADD - 2009

DACE1 sickle thal is linked

David Anthony Cyril Elliman; 28/06/10



Newborn screening in USA - American College of Medical Genetics (ACMG), 2006

“Twenty-nine conditions were identified as primary targets for screening from which all components of the newborn screening system should be maximized. An additional 25 conditions were listed that could be identified in the course of screening for core panel conditions.”



Newborn screening in USA - American College of Medical Genetics (ACMG), 2006

Primary/Core (29) – 20 detected by MS/MS,
3 by HPLC or IEF, 6 by unique tests

Secondary (25) – only 2 not detected by a
multiplex platform, most by MS/MS



Incidental Findings

- “It is important to note that two approaches are currently being used in screening with MS/MS. A majority of screening laboratories now run full profiles that allow them to visualize the full range of acylcarnitines or amino acid compounds. However, a minority operate their systems in a selective reaction monitoring (SRM) mode, which allows them to obtain results only on the subset of compounds that are associated with those conditions that are being targeted in the screening programs.”

ACMG 2006



Incidental Findings – different approaches

- Measure all
 - Report all
 - Report selectively
- Measure selectively



Newborn screening in USA - American College of Medical Genetics (ACMG), 2006

- “The state of the published evidence in the fast-moving worlds of newborn screening and medical genetics has not kept up with the implementation of new technologies, thus requiring the considerable use of *expert opinion* to develop recommendations about a core panel of conditions for newborn screening.”
- (*Eminence* based rather than *evidence* based.)



Newborn screening in USA - American College of Medical Genetics (ACMG), 2006

- “In addition, early information provides opportunity for better understanding of disease history and characteristics, and for earlier medical interventions that might be systematically studied to determine the risks and benefits. *Multiplex testing and the identification of conditions falling outside of the uniform screening panel provides the opportunity for such conditions to be included in research protocols.* Therefore, the criteria used to include a condition in a mandated newborn screening panel are not necessarily straightforward scientific or clinical criteria, but often involve complex ethical, legal, and social policy decisions.”



Newborn screening in USA - American College of Medical Genetics (ACMG), 2006

- “Although information about conditions for which treatment options are scarce or not yet reported can lead to increased stresses on families and the health care system, early information can also lead to knowledge of the condition for the family, thus avoiding a potential diagnostic odyssey or inappropriate therapies.”



Why the differences?

- Different approaches to making recommendations
 - UK very much based on approval for individual conditions assessed against expanded Wilson and Junger criteria
 - v.
 - Broader approach tends to be based more on the technology



Issues

- State of knowledge about test/condition/treatment/outcome
- Consent and information needed to inform it
- Effect of increasing number of false positives
- Effect of increasing number of false negatives
- Handling of incidental findings
- Opportunity costs
- Equity
- Retention of residual bloodspots



Ethics

“The rules or standards governing the conduct of a person or the conduct of the members of a profession.”



Ethics



Screening and Ethics

- Screening is offered to people who do not suspect they have a disease/condition and have not sought advice/help about that disease/condition whereas
- Most medical care is given to people who have sought advice
- ***The ethical imperative is greater with screening***



Ethics in Healthcare

The Hippocratic Oath

- I SWEAR by Apollo the physician, AEsculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgement, I will keep this Oath and this stipulation.
.....
- I WILL FOLLOW that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to any one if asked, nor suggest any such counsel; and in like manner I will not give a woman a pessary to produce abortion.
- No mention of consent or justice



WMA International Code of Medical Ethics

- A physician shall
 - respect a competent patient's right to accept or refuse treatment.
 - be dedicated to providing competent medical service in full professional and moral independence, with compassion and respect for human dignity
 - strive to use health care resources in the best way to benefit patients and their community.



WMA International Code of Medical Ethics

- A physician shall
 - always bear in mind the obligation to respect human life.
 - act in the patient's best interest when providing medical care
 -

Composed 1949, amended
1968, 1983 and 2006



Ethics in Healthcare – Deontology v. Utilitarianism

- Deontology - Rule based ethical systems
- Numerous sources, including most religions

- Utilitarianism - “The greatest good for the greatest number“
- John Stuart Mill



Ethics in Healthcare – General Principles

- Autonomy – being in control of one's own body
- Beneficence – doing good
- Non-maleficence – doing no harm (“primum non nocere”)
- Justice – being fair and equitable



Ethics in Healthcare – Autonomy

- I must choose what happens to me or, at least, must give consent to anything that happens to me.
- To consent, I need to be informed in a manner that I understand and allows time for consideration
- (But what of the consequences to others of my decision?)



Ethics in Healthcare – Autonomy

- In the case of a child, who gives consent?
 - The parent?
 - The healthcare professional?
 - The State?
- How much information is required?
 - Details of 54 diseases; the reliability of the screening test; the treatment and its outcome?
 - A broad outline of the issues?



Ethics in Healthcare – Autonomy

NHS
UK Newborn Screening Centre
Screening Programmes
PARENTS AND NEWBORN

NSC
UK Newborn Screening Centre

Screening tests for you and your baby

Important information for you to keep with your hand-held maternity records

2010 version

NHS
UK Newborn Screening Centre
Screening Programmes
PARENTS AND NEWBORN

NSC
UK Newborn Screening Centre

Screening tests for your baby

Important information for you to keep safe. Please have it with you for all appointments (including hospital stays) so you can discuss your screening choices.

Newborn information only
For antenatal screening only
supply screening tests for you and your baby

2010 version



What are newborn babies screened for?

All babies are offered screening for phenylketonuria, congenital hypothyroidism, cystic fibrosis, sickle cell diseases and medium-chain acyl-CoA dehydrogenase deficiency (MCADD).

If a baby is thought to have one of the conditions, he or she will need further tests to confirm this. These conditions are explained below.

Phenylketonuria

About one in 10,000 babies born in the UK has phenylketonuria (PKU). Babies with this inherited condition cannot process a substance in their food called phenylalanine. If untreated, they will develop a serious permanent mental disability.

Screening means that babies with the condition can be treated early through a special diet which will prevent severe disability and allow them to lead a normal life.

If babies are not screened, but are later found to have PKU, it may be too late for the special diet to make a real difference.

Congenital hypothyroidism

About one in 4,000 babies born in the UK has congenital hypothyroidism (CHT). Babies with CHT do not have enough of the hormone thyroxine. Without this hormone, they do not grow properly and can develop a serious, permanent, physical and mental disability.

Screening means that babies with CHT can be treated early with thyroxine tablets, which will prevent serious disability and allow them to develop normally.

If babies are not screened and are later found to have CHT, it may be too late to prevent them becoming seriously disabled.

Sickle cell diseases

About one in 2,000 babies born in the UK has a sickle cell disease (SCD). These are inherited diseases that affect the red blood cells. If a baby has a sickle cell disease, their red blood cells can change to a sickle shape and become stuck in the small blood vessels. This can cause pain and damage to the baby's body, serious infection, or even death.

Screening means that babies with SCD can receive early treatment, including immunisations and antibiotics, which, along with parent education, will help prevent serious illness and allow the child to live a healthier life.

What happens to your baby's data after screening? You will be told your baby's result and the result will be sent to your healthcare professional. Identifiable data may be stored by the screening programme and used to monitor and improve screening for sickle cell and thalassaemia. The use of data obtained from sickle cell and thalassaemia screening is governed by the National Information Governance Board¹.

If you do not wish your baby's screening data to be used in this way please contact the sickle cell and thalassaemia screening programme:

email at Radoslavl@nhs.net or by telephone on 020 7846 6634 where you will be able to speak to someone in a language of your choice or at sct.screening@nhs.uk contact us

More information on this work is available at ret-screening@nhs.uk/newborn

Cystic fibrosis

About one in 2,500 babies born in the UK has cystic fibrosis (CF). This inherited condition can affect the digestion and lungs. Babies with CF may not gain weight well, and frequently have chest infections.

Screening means that babies with CF can be treated early with a high-energy diet, medicines and physiotherapy. Although a child with CF may still become very ill, early treatment is thought to help them live longer, healthier lives.

If babies are not screened for CF and they do have the condition, they can be tested later but parents may have an anxious time before CF is recognised.



¹ Section 251 of the NHS Act 2006, Section 251 approval has been given for our audit team to access sickle cell and thalassaemia screening data under strict conditions. You can find more information on this at www.nhs.uk/ukic.



Ethics in Healthcare – General Principles

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- Beneficence – doing good
- Non-maleficence – doing no harm (“primum non nocere”)
- Justice – being fair and equitable



Ethics in Healthcare – Beneficence

- The prime aim is to do “good”, i.e. improve outcome for
- the child,
- the family,
- others



Ethics in Healthcare – General Principles

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Ethics in Healthcare – Non-maleficence

- The origin of “primum non nocere” (“first do no harm”) is unclear
- May have been relevant when medicine could do no good
- Few, if any, useful interventions, that don’t ever do any harm
- The balance with beneficence is important
 - more good than harm



Ethics in Healthcare – Non-maleficence

- Testing for more conditions, especially if rare has the potential to
 - Create more false positives
 - More false negatives
 - Increase medicalisation of pregnancy and the neonatal period



Ethics in Healthcare – General Principles

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Ethics in Healthcare – Justice

- Detection and treatment of a rare disorder may be disproportionately expensive and not cost saving
- Opportunity costs, if resources limited. (Costs are not just the screening test, but also professional and parental education, diagnosis, treatment and follow-up.)
- How and who decides on resource allocation
- QALYs and DALYs, but what about equity (to each according to their needs)?



“Genetic Screening”



Newborn Screening – DNA testing 1

- The ability to test for numerous genetic variations
- May indicate
 - disease states (single gene conditions)
 - propensity to disease
 - drug metabolism in an individual



Newborn Screening – DNA testing 2

- Uncertainty about genotype/phenotype match
- Uncertainty about the capacity to bring about improvement
- Testing for conditions that only manifest in adulthood
- Detection of carriers
- Indirectly testing wider family



Newborn DNA Profiling - 1

- Genetic profiling is feasible and likely to become available commercially in less than 20 years using microarrays
- Before the offer of universal genetic profiling could be considered at a population level, steps would need to be taken to preclude any misuse of information derived from it.
- Genetic profiling is unlikely to be publicly affordable within 20 years.
- For newborn genetic profiling, issues of consent and the welfare of the child are problematic



Newborn DNA Profiling - 2

- Genetic profiling may in the future have clinical potential but its effectiveness cannot yet be judged.
- There is a pressing need to develop a programme of research to define the full costs and potential benefits of genetic profiling for the health of children and adults.
- Genetic profiling cannot be applied as an NHS screening programme in the near future.
- The topic should be kept under review and be revisited in five years.

Profiling the Newborn. HGC/NSC 2005



In conclusion

- Increasing technological advances lead to the potential to screen for ever more, but usually less common and poorly understood conditions.
- Many children and their families will benefit from this.
- But this could lead to
 - Insufficiently informed consent
 - Increased anxiety and unnecessary treatment
 - Diminishing returns for increased resource utilisation



The Technological Imperative

- “I must also emphasise at the outset that not everything that can be done should be done. The experts’ role is to research, report and advise. The choice of application must be subject to democratic process.”

Society and the Human Genome. John Sulston. 2002



The Changing Moral Focus of Newborn Screening

An Ethical Analysis by
the President's Council on Bioethics



December 2008

“Hitherto, for diseases that were poorly understood or for which no effective treatment was available, we as a nation have not been in the habit of subjecting individuals to compulsory screening merely for research purposes. In the wake of the ACMG report and its enthusiastic reception by the states, our approach to newborn screening seems to be heading into uncharted territory.”



The Changing Moral Focus of Newborn Screening

An Ethical Analysis by
the President's Council on Bioethics



December 2008

“Therefore, the Council recommends that the states mandate newborn screening only for diseases that meet traditional criteria, including the availability of an effective treatment. But the states are encouraged to implement pilot studies for newborn screening of conditions that do not meet the traditional criteria. Participation in these pilot studies should require the voluntary, informed consent of the infant’s parents. “



The Changing Moral Focus of Newborn Screening

An Ethical Analysis by
the President's Council on Bioethics



December 2008

“In this way, the present benefits of newborn screening can be optimized in an ethical way, and the future benefits of new techniques to expand our knowledge of untreatable diseases will be facilitated in an ethically sensitive way.”



Screening Criteria

- Important condition with known natural history
- Presymptomatic stage
- Accurate screening test
- Available “treatment”
- Acceptable programme