Europe plays catch-up on neonatal screening as US skips ahead

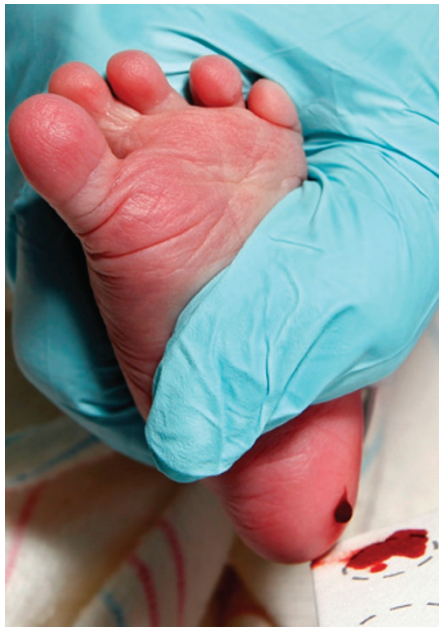
It's a case of transatlantic drift. In September, when the American College of Medical Genetics and Genomics (ACMG) announced the launch of a new centralized virtual repository of newborn dried blood spots, an envious EU looked on, its national constituents unable to agree even on which conditions newborns should be screened for. But things are beginning to change. There are now concerted efforts underway by European health professionals to redress this lack of harmony, and, in mid-November, specialists on newborn screening from across the continent will meet in Brussels, the home of the European Parliament, to discuss the first concrete steps needed to bring into line member states' policies on such tests.

The US has led the world in newborn screening ever since the 1960s, when microbiologist Robert Guthrie, then based at the Buffalo Children's Hospital in New York, first devised an ingeniously simple test for the metabolic disorder phenylketonuria. Guthrie's sampling method—a small prick to a baby's heel to collect drops of blood onto filter paper—is still used worldwide today (although back then phenylketonuria was still screened for using a culture-based bacterial assay).

Today, the introduction of tandem mass spectrometry to look for telltale enzymes and other molecules in the blood has expanded the number of genetic diseases screened for in the US to include a core of 29 conditions, tested on a mandatory basis in every newborn across the country as part of state-based public health programs. The picture in Europe, by contrast, couldn't be more different.

Even within a small country such as Belgium there are notable discrepancies in screening practices between regions, says KU Leuven's Pascal Borry, a bioethicist who, together with VU University Medical Center's Martina Cornel, will convene the meeting on 19 November in Brussels. In the French-speaking south of the country, the regular newborn-screening panel consists of seven conditions, compared with 11 in the Flemish north, Borry explains. Variation among EU countries is even starker: Austria screens for a total of 29 conditions, whereas Finland screens for just one, congenital hypothyroidism.

The differences run much deeper than the individual countries' screening panels. In the first ever comparative study of newborn-screening practices in Europe, released by the EU late last year, Cornel and other scientists found that even the thresholds of metabolites used for screening the same disorder are different not only across countries but also between screening laboratories within the same country.



J. Scott Applewhite/Associated Press

On the spot: Europe's newborn screening.

Screen test

In the US, national newborn-screening standards were established in 2010, just four years after the publication of pivotal recommendations from the Bethesda, Maryland-based ACMG (*Genet. Med.* **8**, 1S–252S, 2006). But cultural hurdles and the vagaries of European politics mean that harmonization of newborn testing, if it can ever be achieved in Europe, presents a tougher challenge. Adding further complications, procedures related to obtaining informed consent, storing samples and using them in research vary from country to country across the EU. As such, forging a consensus on newborn screening is going to take considerable patience, says Gerard Loeber, past president of the International Society for Neonatal Screening (ISNS) in Amsterdam.

"Ideally, policy makers on the level of the EU would sit together and come to consensus," says Loeber, who still serves on the ISNS's governing council. However, he continues, "as long as member states refuse to transfer some power to Brussels, policy makers on the EU level cannot proceed".

Cornel contends that the goal should not be a single EU-wide decree on newborn screening. Instead she argues that efforts should be focused on developing best-practice guidelines that member states can adapt to fit their own health systems and, in some cases, legal systems. Rules governing informed consent, for example, are deeply embedded in national laws and are unlikely to be amenable to change in the short or even medium term, she explains. But there are aspects of newborn screening, such as the assessment of new screening techniques, education, counseling, follow-up and oversight, that might lend themselves to high-level, EU-wide organization.

Even in the US, the establishment of minimum national newborn-screening standards two years ago has not led to a complete standardization of screening practices. In addition to the core 29 conditions there is a 'secondary panel' of 25 further conditions, from which states can pick and choose what to screen for. In some cases, states have started to screen for conditions not included in either of the recommended primary or secondary panels. For example, Illinois has begun screening for Pompe disease, contrary to advice from the Advisory Committee on Heritable Disorders in Newborns and Children within the US Department of Health and Human Services. And Utah is gearing up to start testing for spinal muscular atrophy, despite the lack of proven therapies (see page 1602).

Cornel says that the EU should seek a model with this type of flexibility. "Europe can take note that harmonized, top-down recommendations might work towards promoting a high-quality, basic package, rather than towards dictating totally uniform practices," she says.

Meanwhile, the US continues to forge ahead with fresh innovations in newborn screening. In August, the US National Institutes of Health announced that it was canvassing for research on how best to integrate genomic sequencing into the country's harmonized newborn-screening program. And last month a team largely based out of the Children's Mercy Hospital in Kansas City, Missouri, reported that they had developed a rapid, 50-hour test for genetic disorders using whole-genome sequencing, intended to be used in neonatal intensive care units (*Sci. Transl. Med.* **4**, 154ra135, 2012). What form Guthrie's legacy takes in the decades to come will depend on how society, and the regulators it appoints, answers the many questions posed by these new and constantly evolving screening technologies.

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