excess of surrogate markers of perinatal infections in preterm and term babies who were later found to have cerebral palsy, although the extent to which these associations reflect direct causal effects is unclear.⁶

Gibson and colleagues report how they used the South Australia newborn screening register to retrieve the dried blood spots that had been taken from neonates who were subsequently notified to the local cerebral palsy register and from controls.³ In most developed countries these blood spots are samples taken from all babies after birth to screen for phenylketonuria. They are often retained on Guthrie cards. The South Australian study used such samples to measure the prevalence of the nucleic acids of enteroviruses; herpes simplex virus types 1 and 2; Epstein-Barr virus; cytomegalovirus; human herpesviruses 6, 7, and 8; and varicella zoster virus. The tests were not quantitative, and viral load—which may determine risk of fetal infection—was not measured.

The authors found viral nucleic acids in a high proportion of spots taken from controls: 40% tested positive for at least one. The controls had been matched to the cases by place of care, and the study included an unduly high proportion of babies born in metropolitan teaching hospitals and born preterm. Even so, the prevalence of viral nucleic acids was very much higher than expected from previous epidemiological work.

For instance, 26.7% of the control blood spots tested positive for cytomegalovirus. Studies in London teaching hospitals in the 1980s found positive cell cultures for cytomegalovirus in 3/1000 newborns, looking at samples derived from neonatal throat swabs in one study⁷ and searching for viruses in urine in another.⁸ However, as the Australian authors point out, the prevalence they report does not reflect active fetal infection; it may reflect perinatal exposure to viruses. Moreover, the results may vary with the age of the babies when tested and with methods of storage and retrieval of samples. And the high prevalence may reflect non-specific signals, given that the investigators were co-amplifying multiple viral nucleic acids in very small samples.

Despite these differences from expected absolute prevalence, the reported risks are consistent with those from previous work. The excess of positive tests for cyto-

megalovirus in preterm compared with term controls was significant (odds ratio 1.6). In the sample as a whole, and in babies with gestational age of 37 weeks or more, there was a significant association between a positive test for any viral exposure and cerebral palsy, but also some distinctive associations with different viruses. The authors postulate that, if the associations were causal, 4-5% of all cases of cerebral palsy in these babies might be attributable to perinatal exposure to a group of viruses including human herpesviruses 6 and 7 and varicella zoster virus.

The research group plan to follow this study with prospective and clinical investigations, looking also at interactions with other contributory factors. Overall this is an interesting and provocative contribution to the growing body of research into the role of maternal and fetal infections in cerebral palsy, even though it is based on methods that need further validation.

Eva Alberman *professor emeritus of clinical epidemiology*

(kenevalb@aol.com)

Centre for Environmental and Preventive Medicine, Wolfson Institute of Preventive Medicine, Barts and The London, Queen Mary's School of Medicine and Dentistry, London EC1M 6BQ

Catherine Peckham *professor of paediatric epidemiology*

Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, London WC1N 1EH

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Introducing new health interventions

There's still a long way to go to get health technology evidence into practice

Throughout the world, healthcare innovations have put pressure on limited resources while governments and patients have demanded top quality, yet cost effective, services. This makes it increasingly difficult for anyone who plans, provides, or receives health services to judge which intervention to use—what works, how well, at what cost, for whom, in what circumstances, and with what impact? Health technology assessment (HTA) is a multidisciplinary specialty whose purpose is to bring together the evidence to answer those questions.¹ It boasts a thriving international scientific society (Health Technology

Assessment International; www.htai.org) and a global network of more than 40 public sector agencies (International Network of Agencies for Health Technology Assessment; www.inahta.org). It evaluates the costs, effectiveness, and sometimes the wider impact of any intervention used in the care of patients, including medicines, devices, techniques, and skills. In the UK, for example, the HTA programme (www.ncchta.org) has produced more than 300 reports that have had an

Analysis and comment
pp 107, 109, 112

Figure on bmj.com

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impact on services, including novel research as well as syntheses of evidence on cost effectiveness on topics ranging from left ventricular assist devices to isolation procedures for containing *Staphylococcus aureus*.²⁻⁵ It also provides much of the evidence base for the guidance which the National Institute for Health and Clinical Excellence (NICE) provides for the NHS.⁶

As the bridge between science and policy, HTA examines effectiveness and cost effectiveness in the real world, rather than efficacy in rigidly controlled trials. In the United Kingdom a distinction has emerged between assessment—the supposedly objective scientific summation of evidence about effectiveness—and appraisal, which is a value based judgement made by policy makers such as NICE, who must also consider the ethical, organisational, political, and social impact of technologies. Health technology assessors in many other countries, however, incorporate wider views about relative priority, equity, acceptability and feasibility in their assessments.

Three articles in this issue (pp 107, 109, 112) illustrate just why the assessment and appraisal of health technology is increasingly in demand.⁷⁻⁹ They also show its difficulties and constraints. The social processes of diffusion can turn “technology creep” into widespread practice before health technology assessors can even define, let alone evaluate, new healthcare interventions; but those same processes can result in important developments being ignored or under-resourced.⁹ The trio of articles highlights too how conflicting interests with deeply held values inevitably affect every stage of healthcare innovation. From their early development, through trials and evaluations to policy formulation and practical implementation, new interventions are fought over—often in the full glare of the media—by bodies as disparate as manufacturing industry, patient groups, politicians, insurers, professional bodies, service providers, clinicians, and of course patients.

However objective it tries to be, HTA is subject to these same social pressures. Moreover, its detailed epidemiological and economic analyses are often pitched into a highly political environment where decisions are overwhelmed by broader contextual considerations that receive little if any of the dispassionate methodical analysis afforded to the technical aspects of the intervention. For instance, drug eluting coronary stents were approved by NICE for use in perhaps 30% of coronary angioplasties, and even though this was already more than HTA suggested was appropriate, such stents have been used in as many as 70% of such procedures. Other examples include the controversies over drugs such as interferon beta for multiple sclerosis or trastuzumab (Herceptin) in early breast cancer.

The trade off between the need for rigour and generalisability on the one hand and context-specificity and immediacy on the other, means that HTA faces increasing challenges in delivering analyses that are scientifically robust yet relevant to policy. Methodological challenges fall into three areas.

First is the requirement to identify the technologies that most need assessing: drugs alone are introduced at a rate of almost one novel chemical entity per week. With limited resources for HTA

which new surgical interventions should be assessed and at what stage of their development—neither so early as to waste effort on those that change or never take root, nor too late to avert a fad? The second challenge is a need to develop increasingly sophisticated methods for robust assessments of rapidly evolving technologies, of devices—which often have limited supportive evidence, and of programmes such as diagnostics and screening where clinical and cost effectiveness depend on a chain of diagnostic and therapeutic decisions.¹⁰ Changes in the organisation of service delivery also stretch conventional methods of clinical and economic evaluation such as trials and economic modelling, particularly if policy makers start to call also for assessments of the ethical and other wider aspects of technologies. Thirdly, there is the challenge of implementing HTA findings, which not only faces the usual problems of encouraging the uptake of research into practice but also relies deeply on the nature of the healthcare system and is exceptionally vulnerable to pressure from interested groups.

Technological innovations drive modern health care at an accelerating pace.¹¹ Researchers in HTA must provide robust, relevant, and accessible assessments, and practitioners, patients, and policy makers must engage in that process and use the results. On the evidence of the three papers in this issue, there is still a long way to go.

John Gabbay *emeritus professor*

(jg3@soton.ac.uk)

Wessex Institute for Health Research and Development, University of Southampton, Southampton SO16 7PX

Tom Walley *professor of clinical pharmacology*,

Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool L69 3GF

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