fetal infections, maternal thyroid and nutritional deficiencies, placental disorders, and genetic diseases including Prader-Willi and Angelman’s syndromes, Rett’s syndrome, myotonic dystrophy, non-ketotic hyperglycaemia, thrombophilic disorders, brain malformations, and family history of epilepsy.1,2 In the Western Australian study, 28% of infants with encephalopathy had birth defects compared with 4% of controls, and these defects were judged to have contributed to the encephalopathy in 37% of these cases.10

The relative distribution of causes for encephalopathy may differ by region of the world and level of medical care. Although the incidence of moderate or severe encephalopathy in newborn babies reported in recent case-control studies from Western Australia and Nepal was identical (3–5/1000 term livebirths), 60% of term infants with encephalopathy in Nepal had intrapartum asphyxia or other intrapartum risk factors, by contrast with less than 30% of cases from Western Australia.11 Mortality associated with encephalopathy in Nepal was also threefold higher than in Western Australia (31% vs 9·1%). However, both studies reported that maternal thyroid disorders and infection were major antepartum risk factors for neonatal encephalopathy.

What has been lacking in previous studies is modern MRI of the brain during the neonatal period. The large series reported in this issue of *The Lancet* by Frances Cowan and colleagues from two centres in the UK and Netherlands answers this need and suggests that this modality is useful. In the total series of 351 infants, 77% had evidence of acute hypoxic ischaemic lesions, focal infarctions, or haemorrhages, but only 1% had evidence of old lesions on imaging or autopsy. One interesting feature of the study was the high rate of focal infarctions or haemorrhages in infants with seizures who did not meet other criteria for encephalopathy (69% of 90 infants). Although most investigators and studies such as the Western Australian study have generally lumped infants with seizures alone into a group with other signs of encephalopathy, Cowan and colleagues split their patients into two groups: one with signs of encephalopathy (abnormal tone, feeding, and alertness plus signs of fetal distress) with or without seizures, and another with seizures but no other signs of encephalopathy. The seizure-only group was especially likely to have arterial seizures but no other signs of encephalopathy. The arterial seizure-only group was especially likely to have arterial

#### Commentary

**To treat or not to treat? Implementation of DOTS in Central Asia**

Walk through one of the overcrowded tuberculosis hospitals in Karakalpakstan, Uzbekistan, and the reality of the devastation wreaked by this global pandemic is all too apparent. A high incidence of tuberculosis (new case notification rate 261/100,000 per year) exacts a heavy toll on a population already suffering the economic and environmental effects of one of the worst man-made disasters of the twentieth century: the desiccation of the Aral Sea.1 Médecins Sans Frontieres arrived in the region in 1997, and began a DOTS (directly observed treatment, short course) treatment programme in collaboration with local tuberculosis services. However, in Uzbekistan only the lucky get DOTS. Only 7% of Uzbekistan’s population are covered by the DOTS strategy.2 Indeed, globally, WHO has recently acknowledged that the pace of DOTS expansion has fallen below expectation. The 70% case-detection target will now not be reached until 2013, not 2000 as originally planned.3

The unlucky in Uzbekistan, and much of Central Asia, still receive treatment under the pre-DOTS Soviet-style treatment system. Once a strong system, the break-up of the former Soviet Union in 1991 sent the health services of the Central Asian states into rapid decline.4 Treatment now involves widely varying and often inadequate drug.....
impossible and the alternative to DOTS is dangerously resistant tuberculosis render reaching this target invalid in Central Asia, where high rates of multidrug-negative smear-positive cases. However, this argument is assessed by reaching the WHO target of 85% success for only happen when all the conditions are exactly right, assessed by reaching the WHO target of 85% success for new smear-positive cases. However, this argument is invalid in Central Asia, where high rates of multidrug-resistant tuberculosis render reaching this target impossible and the alternative to DOTS is dangerously inappropriate.

Uzbekistan’s failing tuberculosis system is undoubtedly contributing to some of the highest rates of multidrug-resistant tuberculosis yet recorded in the world; 13% of new patients presenting to Médecins Sans Frontières clinics in the Karakalpak region have multidrug-resistant tuberculosis. In this context, the introduction of DOTS, with an assured drug supply, standardised regimens, and its effect on the priority given to tuberculosis, is a vast improvement; even with its attendant constraints. Given the constraints, DOTS will prevent the continued large-scale emergence of multidrug-resistant tuberculosis.

In addition to drug resistance, the deteriorating Soviet system has created. Nowhere is the need to rapidly expand the DOTS programme more evident than in this region. There is an urgent need for context-specific discussion around these issues, a need already acknowledged by WHO, leading to an improved strategy to tackle tuberculosis in areas with high levels of multidrug-resistant disease. This strategy should include appropriate individualised treatment regimens for retreatment cases in this context. Conflicting opinions from experts, a lack of clarity in many areas of the DOTS protocol, and limited international discussion over the practical considerations of treating a disease that is set to kill 30 million people in the next decade leaves those working on the ground unsure of the best way to assist the populations at risk.

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