

responses were achieved in 27% (n=25) and 28% (n=8) of patients, respectively, over 52 weeks, and responses improved over time. Methotrexate was effective for nail disease as measured by the Nail Psoriasis Severity Index.

Warren and colleagues' results are similar to those obtained in trials comparing methotrexate to biological therapies, in which response to methotrexate was 45%.³ These response rates are lower than the PASI 75 response rates of 60–80% and the PASI 90 response rates of 44–60% reported with biological therapy, especially with infliximab, adalimumab, ustekinumab, and, more recently, the anti-interleukin-17 drugs secukinumab and ixekizumab.^{6–11} Unfortunately, the present study did not compare oral with subcutaneous administration. However, Warren and colleagues' results compare favourably with those of a previous 52 week study showing PASI 75 responses to oral methotrexate (5–25 mg/week) of 24% and PASI 90 responses of 18%, suggesting that subcutaneous administration is superior to oral administration in the management of psoriasis.¹¹ Moreover, the biopsy results confirm the clinical effect, showing reduction of inflammatory cells and reduction of T-helper-17 mediated cytokines.

The question that remains is whether methotrexate should remain the first-line systemic therapy for moderate to severe psoriasis. Because we now know that psoriasis is not just skin deep, and that many of the comorbidities, including psoriatic arthritis, metabolic syndrome, and cardiovascular events, in addition to premature death, are related to the extent of skin involvement, perhaps drugs that effectively control inflammation should be used initially.¹² This approach could only be addressed via long-term observations of prospective studies of patients treated with methotrexate compared with those treated with biological therapy, with collection of information not only about clinical improvement of skin disease, but also about comorbidities. Warren and colleagues' study provides

information about high-dose subcutaneous methotrexate, but only in the short term; long-term follow-up would provide information about sustainability and maintenance of disease control, and prevention of comorbidities.

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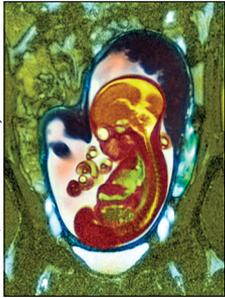
Brain abnormalities in fetuses: in-utero MRI versus ultrasound



Prenatal imaging for diagnosis and prediction of neurodevelopmental outcomes in fetuses with brain malformations is a substantial challenge. Accurate diagnosis of brain abnormalities has important therapeutic implications. Consequently, it is essential that tools used for prenatal diagnosis are rigorously evaluated.

The standard of care is prenatal ultrasound, but in-utero MRI (iuMRI) has been a developing adjunct to prenatal ultrasound for the past 20 years.¹ This process is increasingly used to image the fetal brain after anomalies are recorded during screening or diagnostic prenatal ultrasounds. The most common brain malformations

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in which iuMRI is used include mild ventriculomegaly, agenesis of the corpus callosum, and defects in the posterior fossa. Proponents for iuMRI have argued that it offers clinicians greater visualisation of the ventricular walls, germinal matrix, and developing white matter, and improved tissue contrast compared with conventional ultrasound.² iuMRI might provide additional information that greatly informs patient counselling and clinical decision making. However, iuMRI also has its drawbacks. In centres where specialised neurosonography is available, iuMRI might offer limited improvement to clinical decision making.³ Moreover, iuMRI might have limited accuracy before 24 weeks of gestation, the gestational age at which pregnancy termination is often restricted. Finally, no cost-effective assessment has been done to determine how iuMRI impacts the health-care system. The excellent MERIDIAN study⁴ published in *The Lancet* goes a long way to addressing these questions.

The MERIDIAN study was a multicentre, prospective cohort trial aimed to assess the ability of iuMRI to improve diagnostic performance, clinical impact, and acceptability for patients. 911 fetuses were recruited from 16 sites across the UK, of which 829 had a successful iuMRI. Most fetuses (369 [65%] of 570 who had iuMRI within 2 weeks) were less than 24 weeks gestation. Fetuses with identified intracranial abnormalities on ultrasound underwent iuMRI, mostly within 2 weeks of the ultrasound scan. An interesting component of the design is that radiologists doing iuMRI were not masked to the ultrasound diagnosis. Patients were also unblinded to the modality. Although this approach might introduce bias when determining which imaging modality is more accurate for prenatal diagnosis, it is reflective of clinical practice. Additionally, the radiologists were explicitly expected to compare the results of the different modalities, and these results were compared with the outcome reference diagnosis from post-mortem MRI, autopsy, postnatal CT, postnatal transcranial ultrasound, or postnatal MRI. Despite this methodological framework and its limitations, the results are clear and important.

The primary finding is that diagnostic accuracy of iuMRI with respect to the outcome reference diagnosis improves by 23% (95% CI 18–27) up to 24 weeks gestation and by 29% (23–36) at 24 weeks and older when compared with ultrasound. Although that in itself is statistically significant, these findings also have important clinical implications that were characterised in the study. The

radiologists had greater diagnostic confidence in the iuMRI and this translated into changes in the prognosis offered to the families. These changes moved the prognosis from a category of uncertainty. Crucially, there were almost as many changes to a favourable prognosis group as there was to an unfavourable prognosis group. Unsurprisingly, patient counselling was also affected by the increase in proportion of patients who were removed from categories of uncertainty and there was an increase in the number of terminations of pregnancy that were offered. Overall, iuMRI was acceptable to the mothers with 95% of mothers willing to have an iuMRI in another pregnancy.

These headline findings are important, but there are details that are not available in this Article. For example, there are no example images of how diagnoses and prognoses changed with iuMRI and no details on exactly how diagnoses changed.

It will be important to follow these children through paediatric neurology clinics to map the original structural abnormalities onto later developmental and neurological outcomes. These findings will ultimately refine the ability of fetal medicine providers to prognosticate accurately and reliably offer terminations of pregnancy. An important question remains; if iuMRI is diagnostically superior to ultrasound scanning then there are probably fetuses with normal ultrasound scans that have significant structural abnormalities on iuMRI. However, it is currently not feasible to scan all pregnancies with MRI and it is unclear whether the health economics will ever justify such an approach. Nevertheless, MERIDIAN strongly supports the view that iuMRI is an excellent technique, and it should be incorporated into clinical practice as soon as possible.

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The Trump global gag rule: an attack on US family planning and global health aid

On Jan 23, 2017, on his fourth day in office, President Donald Trump signed an executive order imposing the global gag rule,¹ an anti-abortion policy that under other conservative presidential administrations has caused serious disruptions to US overseas family planning efforts. Alarmingly, Trump's order goes even further than in the past, with potentially devastating effect.

The global gag rule, also known as the Mexico City policy, was devised in 1984 by the administration of Ronald Reagan to impose a draconian set of anti-abortion rules on US overseas family planning programmes.² This policy banned US family planning funds from going to foreign non-governmental organisations (NGOs) that provide abortion services, counselling, or referrals, or advocate for liberalisation of their country's abortion laws—even if they use non-US government funds for these activities. In 1984, and every time the global gag rule has been imposed since then, foreign governments were exempt for diplomatic reasons, as were US-based NGOs on constitutional grounds.

To be clear, legislation was already in place in 1984, and is still in place now, that bans the use of US funds under the Foreign Assistance Act from paying “for the performance of abortion as a method of family planning”.³ But for anti-abortion activists this Helms Amendment, passed in 1973, did not go far enough; they wanted to limit any activity that could possibly enable or promote abortion. Hence, the global gag rule.

Under Trump's order, the gag rule now applies not only to US bilateral family planning assistance (US\$575 million for fiscal year 2016),⁴ but also to all “global health assistance furnished by all departments or agencies”¹—encompassing an estimated \$9.5 billion in foreign aid.⁵ Foreign NGOs that receive US funding to work on a broad range of health programmes in about 60 low-income and middle-income countries—including on HIV/AIDS, the Zika virus, malaria, tuberculosis, nutrition, and maternal and child health, among others—will potentially

be subject to the same ideological restrictions that have hampered family planning aid at points in the past.⁶ Thus, President Trump's version of the global gag rule represents a wider attack on global health aid writ large.

Adding to the widespread concern among US government agencies, global health NGOs, and advocates is the Trump administration's failure to provide any guidance on the interpretation or application of the new policy. Those details may emerge in the coming weeks and months. But we already know that, when last in effect, the gag rule crippled family planning programmes. Many foreign NGOs, as a matter of principle and out of dedication to the patients they serve, refused to let the US Government muzzle their abortion advocacy efforts or dictate what services or counselling they provided using their non-US funds. These health providers were forced to reduce staff and services, or even shut clinics.² As a result, many thousands of women no longer had access to family planning and reproductive health services from these clinics—sometimes the only provider of such services in the local community. Various actors, including the governments of Canada and the Netherlands, are mobilising to compensate for at least some of the damage that will be done by the gag rule. But the US is the largest funder of global health programmes worldwide,⁷ and the disruption this aid effort will suffer is massive.

Moreover, there is no evidence that the global gag rule has ever resulted in its stated aim of reducing abortion. The first study to measure the effect of the gag rule showed that this policy could actually have resulted in an increase in abortions.⁸ Another study assessed the gag rule in Ghana and found that because of declines in the availability of contraceptive services, both fertility and abortion rates were higher during the gag rule years than during non-gag rule years in rural and poor populations.⁹ This is consistent with anecdotal data that the gag rule's main effect has been to reduce women's access to quality contraceptive services, thereby

