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Predicting pre-eclampsia: 100 years of trying and failing

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The symptoms of eclampsia, a Greek word meaning 'lightning', have been known to medicine since Hippocrates (460–370 BC), but it was only in the 18th century that doctors made a distinction between eclampsia and epilepsy (Bell MJ. *J Obstet Gynecol Neonatal Nurs* 2010;39:510–8). Eclampsia/pre-eclampsia results from a disorder of placentation characterised by the insufficient transformation of the spiral arteries at the level of the placental bed. The trophoblastic invasion is sufficient to allow early pregnancy phases of placentation, but is too shallow for the complete transformation of the arterial uteroplacental circulation. Heritable paternal imprinting of the genome is necessary for normal trophoblast development. Several large cohort studies have identified paternal single nucleotide polymorphisms (SNPs) that have strong associations with pre-eclampsia, in particular in the paternally expressed genes affecting placentation (Dekker G et al. *J Reprod Immuno* 2011;89:126–32). We have proposed that eclampsia/pre-eclampsia is a three-stage disorder, with the primary pathology being an excessive or atypical maternal immune response, which impairs placentation leading to placental chronic oxidative stress, and subsequently to diffuse maternal endothelial cell dysfunction (Jauniaux E et al. *Hum Reprod* 2006;12:747–55).

For centuries the diagnosis of eclampsia or toxaemia was exclusively based on the presence of maternal convulsions, before or after delivery. Other symptoms such as headache, hypogastric pain, temporary loss of vision, and severe oedema were recognised by the mid 19th century, suggesting that a prodromal stage existed before eclampsia. Pierre Rayer (1793–1867), a French physician, was the first to describe proteinuria in eclamptic women and John Lever (1811–1859), an English physician, is credited with being the first to have shown that eclampsia-associated proteinuria was specific to the disease (Bell MJ. *J Obstet Gynecol Neonatal Nurs* 2010;39:510–8). Modern blood pressure measurement became available when Nikolai Korotkov (1874–1920), a Russian vascular surgeon, discovered the difference between systolic and diastolic blood pressure. Urine analysis and blood pressure measurements came into use at the beginning of the 20th century (Corbett D *BJOG* 1913;23:227–37). These discoveries made it possible to identify women at risk of eclamptic convulsion, and the concept of pre-eclampsia started to appear in modern medical literature.

Eclampsia remains a major cause of maternal mortality in developing countries, but in developed countries screening programmes including routine blood pressure measurements and urinalysis were introduced in the 1960s to detect pregnant women at the pre-eclamptic stage. The development of Doppler ultrasound in the 1980s and more recently the use of new maternal serum markers have made limited alterations in the management of pre-eclampsia. A recent systematic review of studies reporting risk prediction models for pre-eclampsia, including uterine Doppler measurements, has found frequent methodological deficiencies, thus limiting their reliability and validity (Brunelli VB et al. *BJOG* 2015;122:904–14). Risk factors for pre-eclampsia such as kidney disorders, diabetes, chronic hypertension in multiple-gestation pregnancy, and a previous history of pre-eclampsia have been identified over the last four decades, but for the general population of pregnant women the screening and management of pre-eclampsia has changed very little, and is essentially based on observation, antihypertensive drugs, magnesium sulfate (popularised in the 1920s) and delivery before the eclamptic stage.

Disclosure of interest

None declared. Completed disclosure of interests form available to view online as supporting information. ■