## Predicting preeclampsia - one hundred years of trying and failing

The symptoms of eclampsia, a Greek word meaning “lightning” have been known to medicine since Hippocrates (460-370 BC) but it is only in the 18th century that physicians made a distinction between eclampsia and epilepsy (Bell MJ J Obstet Gynecol Neonatal Nurs 2010;39:510-8). Eclampsia/preeclampsia results from a disorder of placentation characterised by 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 too shallow for complete transformation of the arterial utero-placental circulation. Heritable paternal imprinting of the genome is necessary for normal trophoblast development. Several large cohort studies have identified paternal SNPs with strong associations with preeclampsia, 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 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 Toxemia 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 to be 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 started to be 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 preeclampsia started to appear in the modern medical literature.

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

MC to be linked with MS 2015-CM-16132 by Cheong-See et al

**Disclosure of interests**
We declare no conflicts of interest.

Eric Jauniaux
Academic Department of Obstetrics and Gynaecology
Institute for Women's Health
University College London
London, UK

Philip Steer

Emeritus Professor of Obstetrics,
Imperial College London
Academic Department of Obstetrics and Gynaecology
Chelsea and Westminster Hospital
London UK