Debate: The placenta is the villain or victim in the pathogenesis of preeclampsia. FOR: The placenta is the villain in the pathogenesis of preeclampsia.

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In keeping with legal precedent when prosecuting a case, quoting a pithy Latin phrase can often be a winning gambit.

Simply put, therefore, in arraigning the placenta as culpable in the pathogenesis of preeclampsia, *sine qua non* surely does the trick, for without a placenta, there is no preeclampsia. While a fetus or a gravid uterus is usually sufficient for an occurrence of preeclampsia, neither is in fact necessary. Exhibit one, a hydatidiform mole, bears witness to the former contention, and exhibit two, an abdominal pregnancy, to the latter (Redman. *N Engl J Med* 1990; 323: 478 – 480). It is the placenta that is caught red-handed as the culprit.

Moreover, notwithstanding the continuing validity of Paul Zweifel's pronouncement in 1916 (Zweifel, P. Eklampsie. In: Dederlein, A., editor. Handbuch Der Geburtshilfe. Bergman: Wiesbade: 1916. p. 672 – 723) that (pre-) eclampsia is a disease of theories, the overwhelming weight of contemporary research evidence firmly places the placenta front and centre at the scene of the crime (Burton et al. *BMJ*2019; 366:12381.1-15).

While other bodily organs and systems (including renal, hepatic, cerebral, cardiovascular, haematological) may be complicit in the grievous bodily harm (GBH) wreaked upon a pregnancy by preeclampsia, the placenta cannot use their downstream dysfunctions as conviction-avoiding alibis. The placenta is undoubtedly the ringleader and puppet-master of the gang. Modern detective work has shown the placenta exercises its sinister influence by using a large arsenal of weapons (including anti-angiogenic molecules, pro-inflammatory cytokines, and a wide array of necrotic and apoptotic trophoblast microvesicles). Once in circulation, this ordnance attacks the innocent and unsuspecting occasioning the GBH which is the criminal subject of this prosecution (Burton et al. *BMJ* 2019; 366:12381.1-15).

Now it may be proposed that this trophoblastic villainy is to be excused because the placenta at a very young and tender stage of its development may be subject to deleterious, stress-inducing influences (probably parentally immunogenetic in origin). This in turn causes histological and cytological maldevelopment of the placenta which leads to its subsequent malevolent misbehaviour as pregnancy progresses, resulting in preeclampsia (in particular, the early onset type) (Brosens et al.*Am J Obstet Gynecol* 2019; 221(5): 437-456; Huppertz*Hypertension* 2008; 51(4): 970-975). Thus the impact of the placenta under this scenario is predetermined and not primarily of its own making. However, this line of argument cannot be allowed to absolve the placenta of ultimate responsibility for the pathogenesis of preeclampsia. This is because in the so called late onset type of preeclampsia (which is the majority of cases), evidence of early pregnancy insult is less discernible, with placental culpability being more associated with (premature) senescence of the mature placenta (Staff. *J Reprod Immunol* 2019; 134-135:1-10).

Before closing the case for the prosecution, witness impact statements relating to the world-wide and life-long harm associated with preeclampsia should be highlighted

(Duley. *Semin Perinatol.* 2009; 33(3):130-137; Leslie and Briggs.*J Midwifery Women's Health* 2016; 61(3): 315-324).

Therefore, any placenta found guilty as charged in a case of preeclampsia should be sentenced upon conviction to be dissected and then to spend as much time as ethically permitted housed in secure biobank. This may allow eventual redemption in the form of revelations following further interrogation that clarify precisely the placental aetiology of preeclampsia at long last.

Disclosure of interests

No conflicts to declare.

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