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Eclampsia still kills

Fortunately eclampsia is now a rare complication of pregnancy. A general practitioner will probably see only one actual or impending case in a lifetime, yet the safety of his patient may depend critically on how he recognises and responds to the problem. Obstetricians also have little experience to guide them; and their methods of detecting and managing imminent eclampsia are so imperfect that most eclamptic fits still occur in hospital.

Grand mal convulsions distinguish eclampsia from pre-eclampsia, although we do not know if the prodromal disorder is always present before convulsions begin. Even at the time of eclampsia, up to 41% of patients have had little or no proteinuria,[1-3] a sign of advanced pre-eclampsia. Eclampsia usually occurs in the second half of pregnancy, more commonly towards term,[4] but has been observed as early as the sixteenth week.[5] In about half the cases convulsions begin before labour[1 6]; postpartum eclampsia usually occurs within 24 hours of delivery[2] but may present 48 hours to three weeks later.[7 8]

The direct cause of eclamptic convulsions is not known. They are seven to eight times more common in patients who have had pre-eclampsia with proteinuria than without.[9] Extreme hypertension is not a necessary predisposing factor, but the average blood pressures of women with eclampsia are higher than those of women with severe pre-eclampsia,[3] so the relation between the cerebral disease and the hypertension needs to be considered.

The clinical features of eclampsia include proteinuria, renal impairment, and disseminated intravascular coagulation, which are also characteristic of malignant hypertension.[10] But pre-eclampsia and eclampsia are usually not complicated by papilloedema or retinal haemorrhages, and malignant nephrosclerosis is not found at necropsy. Eclampsia thus cannot be classified as malignant hypertension. Instead, it is probably a form of hypertensive encephalopathy—an acute or sub-acute syndrome of diffuse cerebral dysfunction that is not ascribable to uraemia and which is reversed by treating the raised arterial pressure. The encephalopathy rarely complicates malignant hypertension[11] but more often occurs in patients with acute nephritis and, like eclampsia, is not normally associated with gross papilloedema or retinopathy.[12] Eclampsia and hypertensive encephalopathy have many common features including the symptoms of headaches, vomiting, and convulsions and the complication of cortical blindness.[12-14] The pathology in the cerebrum is also similar in the two conditions, comprising thrombosis, fibrinoid necrosis of the arterioles, diffuse microinfarcts, and petechial haemorrhages.[15 16] These changes are not found in malignant hypertension but do sometimes occur in systemic lupus erythematosus.[17]

The importance of cerebral oedema is unclear. It is not seen consistently in eclampsia but has been identified as the cause of about a fifth of deaths.[18] Whereas it was the only cerebral abnormality in 20% of one series of necropsies[19] it was not seen at all in another series.[15] Diffuse and focal cerebral oedema[20 21] have been shown in eclamptic women by computed tomography. The same technique has revealed focal areas of cerebral oedema in cases of hypertensive encephalopathy,[22] even though oedema is not a consistent feature at necropsy.[16] In both conditions the pressure of the cerebrospinal fluid may be increased.[12 23] Focal cerebral oedema can be induced experimentally by extreme hypertension,[24] but the cause of the cerebral dysfunction in hypertensive encephalopathy is not fully understood. One hypothesis is that it is caused by ischaemia secondary to intense vasoconstriction.[15] Vasoconstriction is, however, a protective, not a pathological, response to extremes of arterial pressure[25]; it prevents an uncontrolled increase in tissue perfusion and damage to the distal microcirculation. But at high arterial pressures the vascular smooth muscle may reach the limit of its strength and then yield; short segments give first, but they extend until the length of the vessel is "blown out." This sequence can be shown during extreme experimental hypertension.[24] The dilatation is associated with damage to the vessel wall, with focal oedema around the dilated segments.[26] Thus hypertensive encephalopathy is probably not caused by vasoconstriction but by a loss of tone in the small arteries and arterioles because of pressure. This has not, however, been proved to be the mechanism of eclampsia.

In Britain eclampsia complicates probably fewer than 1 in 1000 deliveries, but its exact incidence is not known. In Oxford eclampsia complicated 0·036% of deliveries in 1978-86. This figure includes some transferred cases, but extrapolation gives an estimate of about 180 new cases every year in Britain. Eclampsia and pre-eclampsia are the most important obstetric causes of maternal mortality in the Western world, including the United States,[27] the Nordic countries,[28] and England and Wales.[29] Cerebral haemorrhage is identified as the lethal event in 50-65% of cases.[19 29] Women who die of eclampsia have significantly higher blood pressures than those who survive but not more proteinuria or worse renal function. Paradoxically, although it is a disease of young women having their first babies, those who die tend to be older and parous.[19]

It should be remembered that deaths from pre-eclampsia nearly equal those from eclampsia[29]: it is not the convulsions that make this condition so dangerous. Eclampsia is conventionally considered to be the end stage of the disorder, but this is an oversimplification. Some patients have only minor systemic disturbances and the problem is easy to control with rapid recovery after delivery. Other patients are desperately ill with progressive renal failure, disseminated intravascular coagulation, microangiopathic haemolysis, and liver dysfunction. Thus convulsions are a marker for severe illness but not a reliable one. Some patients with pre-eclampsia are more dangerously ill than others with eclampsia. Often too much effort is spent in giving treatment to pre-eclamptic women to prevent convulsions (in circumstances where eclampsia is unlikely) and too little in determining the extent and severity of the illness, so that those with severe systemic disturbances can be selected for urgent delivery.

In addition many doctors do not appreciate the chameleon-like nature of this extraordinary condition. The fulminating illness may begin with headaches and vomiting that can easily but dangerously be discounted as "viral gastroenteritis." Jaundice is a rare presentation[30] and is often misinterpreted by specialists. The severity (and therefore dangers) of a pre-eclamptic illness are never reliably shown by a single measurement. It is conventional to equate the degree of hypertension with the extent of the problem. Although this is true in general, there are enough exceptions to make this a dangerous assumption. There is increasing evidence for "normotensive" pre-eclampsia,[31] a condition characterised by intrauterine growth retardation and maternal problems that may include disturbances of clotting and hepatic function.[32-34]

Some rules of thumb are helpful for those trying to cope with this disease in the frontline. Firstly, no consultation with a pregnant woman is complete without a blood pressure measurement and a check for proteinuria. Those with blood pressures of 140/90 mm Hg or more and proteinuria of 1+ or more on dipstick examination should be considered to have advanced disease and admitted to hospital on the same day. Those who are also feeling ill need to be admitted by flying squad. Any pregnant woman suffering from headaches and vomiting in the second half of pregnancy should be assumed to have terminal pre-eclampsia until proved otherwise. In hospital specialist assessment of any case of suspected pre-eclampsia is incomplete without knowing a patient's renal function (measurements of plasma urea and creatinine are good enough), platelet count, and hepatic function (plasma aspartate aminotransferase activity). These investigations need to be constantly available, and all but the last are already provided by most emergency laboratory services. As pre-eclampsia is an unstable condition that may change dramatically regular reassessments are essential. Cure depends on elective delivery.

It is time that doctors took a new look at this major problem of obstetric care. All cases of eclampsia occurring in Britain should be reviewed regularly to provide an analysis and overview of what is happening. With their well established tradition of audit, all obstetricians would surely want to assist such an endeavour, which should lead to better prevention and management.

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Estimating with confidence

The *BMJ* now expects scientific papers submitted to it to contain confidence intervals when appropriate.[1] It also wants a reduced emphasis on the presentation of P values from hypothesis testing.[2] The *Lancet*,[3,4] the *Medical Journal of Australia*,[5] and the *American Journal of Public Health*[6] have implemented the same policy, and it has been endorsed by the International Committee of Medical Journal Editors.[7] One of the blocks to implementing the policy has been that the methods needed to calculate confidence intervals are not readily available in most statistical textbooks. Today the *BMJ* continues a series of articles that aims at filling that gap (p 1238); they will eventually be published as a book. Further articles in the *American Journal of Public Health* and the *Annals of Internal Medicine* have debated the uses of confidence intervals and hypothesis tests and discussed the interpretation of confidence intervals.[8-14]