ACTION ON PRE-ECLAMPSIA PARLIAMENTARY BRIEFING FOR WESTMINSTER HALL DEBATE ON PRE-ECLAMPSIA 9TH MAY 2019 1330-1630

Action on Pre-eclampsia
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Key Policy Asks from Action on Pre-Eclampsia

1 – We welcome the NHS England announcement that Placental Growth Factor PlGF testing will be made available in England and are delighted that the tests have been added to the Accelerated Access Collaborative. We now call on the Government to ensure Trusts deliver on making PlGF testing available on the basis of clinical need throughout the United Kingdom, not just England.

2 – We call on the Government to recognise World Pre-eclampsia Day on 22nd May every year

3 – "Whilst pre-eclampsia causes very few maternal deaths in the UK it is still the cause of many hundreds of stillbirths per year. We call on the government to prioritise research into stillbirths from pre-eclampsia and to increase the resources available to support parents through this trauma."

4 – The UK has the lowest incidence of maternal mortality in the world from pre-eclampsia and we call on the government to note that this is down to excellent care and observation by clinicians over the last 30 years and to recognise that it is not a result of a cure being found.

5 – The last report into maternal mortality (MBRRACE) showed that Black women, compared to White, are 5 times more likely to die in pregnancy and Asian women are twice as likely to die in pregnancy. Black women (compared to White) are around 3 times more likely to develop pre-eclampsia in their pregnancies so we call on the Government to prioritise care for hard to reach and at risk groups and to reduce inequalities in care

6 – We call on the NHS to adopt a "life course focus" instead of just a pregnancy disease focus. Preeclampsia highlights women who go on to have a greater risk of vascular and chronic kidney disease - this gives a window of opportunity to intervene if care between obstetric and primary care is improved. The immediate maternal and neonatal morbidity of pre-eclampsia is apparent. Much less appreciated is the longer-term legacy of adverse post-reproductive health in women who have experienced a pregnancy complicated by pre-eclampsia. Non-communicable diseases such as cardiovascular disease, stroke and end stage renal disease (ESRD) are much more common in women who have experienced pre-eclampsia. This is a lost opportunity for early intervention and targeted preventative strategies.

Further information

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Key Information about the UK and pre-eclampsia

Pre-eclampsia is a syndrome of hypertension, significant protein in the urine and placental dysfunction after the 20th week of pregnancy.

Worldwide;

- Globally pre-eclampsia accounts 14% of all maternal deaths.
- 40,000 women die each year from pre-eclampsia.
- Five women die from complications of pregnancy related to pre-eclampsia every hour
- Limited access to or substandard care in pregnancy is associated with poor outcomes
- The greatest burden is in low income countries
- Pre-eclampsia is a common cause of pre-term birth – baby delivered early they are not growing in the womb or because of complications in the mother such as extremely high blood pressure or kidney failure.
- Increasing maternal age, rates of obesity, insulin resistance and pre-existing hypertension in high income countries are associated with pre-eclampsia

In the UK, good Ante-natal care has made a huge difference to reduce maternal deaths

- The UK has a commission that audits all maternal deaths called MBRRACE
- In 2016 MBRRACE UK reported that British women have a less than 1 in 1 million chance of dying in pregnancy as a result of pre-eclampsia.
- Screening and diagnosis are the cornerstones of safe management
- Maternal deaths secondary to hypertensive disorders in pregnancy are preventable with;
  - ✓ Universal access to routine antenatal care in pregnancy
  - ✓ Regular blood pressure and urine checks
  - ✓ Education about the risk factors and symptoms of pre-eclampsia
  - ✓ Evidence based guidelines for ante-natal care and the management of hypertension in pregnancy

- An Irish academic study in 2017 found the average cost of a pregnancy complicated by preeclampsia was €5243 per case compared with €2452 per case for an uncomplicated pregnancy, we believe the differential to be similar in the UK.

- **Based on the ONS figure of 679,106 live births in the UK in 2017, using an estimate of 5% of pregnancies in the UK being complicated by pre-eclampsia and using the above differential this gives an estimated immediate cost to the UK of £81,428,560**

Even though the UK has very low levels of maternal deaths, there are still high numbers of stillbirths and babies being born prematurely and/or underweight because of pre-eclampsia and many women who are suffering from pre-eclampsia in pregnancy.

About APEC

Action on Pre-eclampsia (APEC, charity number 1013557) aims to raise public and professional awareness of pre-eclampsia, improve care, and ease or prevent physical and emotional suffering caused by the disease.

- We run a helpline and provide information to members of the public who are affected by pre-eclampsia – be this pregnant women, their family and friends and anyone worried about pre-eclampsia.
- We run study days for midwives and health professionals who work with pregnant women, providing expert training on detection and management of pre-eclampsia.
- We organise the UK meeting on hypertension in pregnancy
- We also facilitate a unique expert referral service, whereby women can be referred by their GPs to an expert on pre-eclampsia in their area.
- APEC also provide leaflets to hospitals and maternity units informing women about pre-eclampsia and the importance of antenatal care. We have distributed over 300,000 leaflets this year alone.
- We offer online training for midwives
- APEC is currently seeding patient groups in other countries after successful implementation into Ghana
- This year we have launched a "know the symptoms" campaign fronted by Dr Dawn Harper.
- We receive no government funding
- APEC acts as the Patient and Public Involvement representative on over 30 trials worldwide including most of the larger research projects in the United Kingdom, these include research into the benefits of home blood pressure testing, the James Lind Alliance hypertension in pregnancy work and implementation of low cost blood pressure monitors into low income settings.
- APEC provide subsidised blood pressure monitors which are calibrated for pregnancy and are low cost to over 30 countries worldwide.

https://action-on-pre-eclampsia.org.uk/

Further information

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About Pre-eclampsia

What is pre-eclampsia?

- Pre-eclampsia is an illness arising only in pregnancy which can affect the mother, her unborn child, or most commonly, both.
- It can occur at any time from around twenty weeks to as late as several days after delivery.
- In the mother, the condition causes a number of symptomless disturbances – including raised blood pressure (hypertension) and leakage of protein in the urine (proteinuria) – which can progress to serious illness if undetected.
- The unborn baby may grow more slowly than normal or suffer potentially dangerous oxygen deficiency.

What is the test for pre-eclampsia?

- As yet there is no single diagnostic test for pre-eclampsia.
- Pre-eclampsia is a complex multi-system disease which is diagnosed by measuring blood pressure and checking urine.
- When a woman is diagnosed with pre-eclampsia she is;
    - ✓ admitted to hospital.
    - ✓ given medication to control potentially life-threatening problems like high blood pressure,
    - ✓ an ultrasound to check that their baby is growing normally
    - ✓ blood tests to monitor their kidney and liver function and blood clotting.
- There is no cure for pre-eclampsia, the principle of management of women with pre-eclampsia is
    - ✓ to treat the life-threatening problems,
    - ✓ monitor for complications
    - ✓ plan for delivery.
- Once a woman is diagnosed with pre-eclampsia it is hard to predict the outcome accurately. Some women may need to have their baby immediately, others may be stable for a couple of weeks before delivery.

How common is it – and how dangerous?

- In its broadest form and including gestational hypertension, pre-eclampsia affects as many as one in 10 of all pregnancies, making it the most common of the serious pregnancy complications.
- It occurs more often in first pregnancies, although a minority of women who have suffered it once get it again in one or more subsequent pregnancies.
- Pre-eclampsia is usually mild, but 1-2 in every 100 first pregnancies is so severely affected that there is a serious risk to the life of the baby – and even the mother.
- Every year in the UK many hundreds of babies die **because** of pre-eclampsia – many of these as a consequence of premature delivery rather than the disease itself.
- Some 1-2 mothers die each year from complications of pre-eclampsia in the UK.

Who is most at risk?

- No one can predict with certainty who will get pre-eclampsia.
- Every woman is at greater risk in her first pregnancy, although the risk is higher for those with a strong family history of the complication. Other risks for developing pre-eclampsia include: carrying twins, mothers over the age of 40, mothers who are overweight or obese, or having one of several chronic medical problems, including high blood pressure, kidney disease, diabetes or, to a lesser extent, migraine.

- Some studies have suggested that women of Black and Asian ethnicity are more likely than women of White ethnicity to develop pre-eclampsia but more needs to be done to investigate why this is the case and what can be done to reduce this risk.Women who have had pre-eclampsia in a first pregnancy may get it again. However, those who have enjoyed normal first pregnancies rarely get pre-eclampsia in subsequent pregnancies.
- The risk of repeat attacks is increased if the mother is carrying twins or has one of several chronic medical problems, including high blood pressure, kidney disease, diabetes or, to a lesser extent, migraine.

What causes pre-eclampsia?

- No one knows for sure, although genetic factors are probably involved, since women whose mothers and sisters have suffered pre-eclampsia are more likely to get it themselves.
- What is known is that pre-eclampsia originates in the placenta – the special pregnancy organ which links a mother to her unborn child.
- The placenta needs a large and efficient blood supply from the mother to sustain the growing baby. In pre-eclampsia, the placenta runs short of blood either because its demands are unusually high – as with twins – or because the arteries in the womb did not enlarge as they should have done when the placenta was being formed in the first half of pregnancy.

What happens to the mother?

- Signals from the deficient placenta affect the mother's blood vessels, raising her blood pressure and disturbing her kidney and/or liver function, so that waste products accumulate in the blood, while valuable proteins leak into the urine.
- As the disease progresses, the mother's liver, lungs, brain and blood clotting system can also be affected. Eclampsia (convulsions), cerebral haemorrhage (stroke), pulmonary oedema (fluid in the lungs), kidney failure, liver failure, and breakdown of the blood clotting system (disseminated intravascular coagulation) are the most dangerous complications – all of them fortunately, very rare.

What are the symptoms?

- Headaches
- Swelling of the face, hands, or feet
- Abdominal pain
- Visual disturbances such as flashing lights
- Reduced fetal movements
- Nausea and vomiting

Is there a cure?

- The only cure for pre-eclampsia is delivery of the baby and the placenta.
- Dilemmas arise when early delivery would solve the mother's problems but put the baby at risk of the effects of extreme prematurity.
- Sometimes the clinical manifestation of pre-eclampsia may appear or worsen after delivery.

What treatments are used?

- Mothers are often admitted to hospital if they have pre-eclampsia – which means protein in the urine as well as high blood pressure. This is to enable doctors and midwives to monitor

the progress of mother and baby as closely as possible so that a safe birth is carried out if complications start to set in or when the woman is 37 weeks pregnant or more.

- Pre-eclampsia is progressive – it doesn't get better and usually gets worse. So, once admitted, mothers are not normally allowed home until after their baby has been born. Babies born underweight or early are likely to need to go to the neonatal unit soon after birth which is traumatic for the family.
- Antihypertensive drugs, which reduce high blood pressure, are often prescribed; although we do not think they affect the underlying disease, they can reduce the risk of some complications, such as cerebral haemorrhage. Magnesium infusions also be prescribed to control eclamptic fits.

What happens to the baby?

- As the blood supply from the mother to the placenta is restricted, the baby's supply of nutrients and oxygen may be reduced, leading at first to slower than normal growth (intrauterine growth retardation – IUGR) and later to oxygen starvation and potentially stillbirth.
- Once pre-eclampsia is suspected or known, the unborn baby is monitored as closely as the mother so that the delivery can be carried out before its problems become serious. Decisions about early induction are particularly difficult when a premature foetus (of under 28-30 weeks' gestation) is severely affected by pre-eclampsia but could not be certain of survival outside the womb.

Are there any long term effects?

- For the great majority of mothers, the birth of her baby reverses all the effects of pre-eclampsia, although recovery may take a week or two and blood pressure may often rise just after birth before it falls to normal levels.
- For an unfortunate few, however, some organ damage remains after the disease itself is cured and women will be diagnosed with high blood pressure or kidney disease.
- Studies have shown that women who develop pre-eclampsia in pregnancy, compared to those who don't, are at greater risk long term during of developing cardiovascular disease (high blood pressure, heart attacks and stroke) and kidney disease which also shortens their life expectancy. At the moment in the UK there are no standard care pathways to monitor the long term health of women who have had pre-eclampsia – we believe this needs to be addressed.
- Babies who are born underweight or prematurely due to pre-eclampsia are at greater risk of cardiovascular disease and diabetes in later life. This highlights the need for ongoing research to find better treatments and/or a cure that might reduce these risks for the children of women who suffer from pre-eclampsia.

PIGF – Placental Growth Factor Tests

- The signs and symptoms of pre-eclampsia are not reliable or consistent. Women will therefore often be admitted unnecessarily, or can have severe disease without being diagnosed.

- This is dangerous as severe problems can occur without warning (such as fits and uterine bleeds). Because pre-eclampsia affects many different systems in the body and can present suddenly without warning, it can be difficult to diagnose.

- As well as monitoring blood pressure and checking the urine for protein, blood tests of liver, kidney and clotting function are used to check if the disease has started to cause organ damage in the mother as this can indicate severe disease needing immediate delivery.

- Scans of the baby are also done to ensure the pregnancy can continue safely.

- These tests may be normal and do not indicate whether pre-eclampsia exists or predict whether it will progress rapidly. It can therefore be difficult for the teams of doctors and midwives looking after women with pre-eclampsia to know who can be safely monitored out of hospital and which women have severe disease requiring admission and close surveillance, because there have previously been no tests which can confidently rule out the presence of pre-eclampsia.

- A new blood test (known as PLGF based tests) indicates whether the women has the disease and when used in women with suspected pre-eclampsia can reliably indicate who will need delivery soon. It is a reliable test of whether the baby is at risk. This test can be used to indicate who needs admission and intensive monitoring to determine when delivery is required, or who can be discharged home. Many other tests can frequently be avoided and it is therefore cost effective.

- There are currently 3 versions of these tests available in the UK. All of them measure PLGF, and one also measures SFlt, and uses it as a ratio with PLGF. The PLGF is not the same in each assay, as there are 4 subtypes (isoforms) and each assay measures them differently. Each test is equally valuable, but has different levels to indicate action.

- These tests will be available in the NHS, and the clinicians will be aware of which values to use. If the test is normal in women with worrying features, it is unlikely that pre-eclampsia will develop. If the test is abnormal, then more monitoring can be instigated to both mother and baby and delivery arranged when appropriate. Blood pressure may be treated in the meantime and drugs (magnesium sulphate) given while delivery is being arranged.

- At the moment PLGF based tests reliably indicate who does not need delivery.

- The three tests are owned by Roche, Perkin Elmer and Quidel.

- **APEC takes no position on individual tests other than supporting implementation across the NHS.**

Information from the three PlGF companies.

APEC invited each company to comment on their product.

Perkin Elmer

The NIHR funded SPREE study (1) established that the performance of screening for Pre-eclampsia as currently recommended by NICE guidelines is poor and compliance is low. The performance of screening can be substantially improved by a method combining maternal factors with biomarkers including PLGF, during the 1st Trimester. The ASPRE trial (2), demonstrated that identifying women at high risk using this approach, followed by treatment with Aspirin, started before 16 weeks gestation, could significantly reduce pre-term Pre-eclampsia by more than 60%. The study also demonstrated a 65% reduction in the length of stay in Neonatal Intensive Care. (3)

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3. Wright *et al,* 2018 *:* Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin on length of stay in the neonatal intensive care unit. Am J Obstet Gynecol. 2018 Jun;218(6):612.e1-612.e6. doi: 10.1016/j.ajog.2018.02.014. Epub 2018 Mar 2

Quidel

In May 2016, the National Institute of Clinical Excellence (NICE) recommended that Placental growth factor (PlGF) based tests be used to help diagnose pre eclampsia. In April 2019, The Lancet published a 1035-patient implementation study conducted in England which demonstrated improvements to cost and clinical outcomes; PlGF-guided care achieved a 64% reduction in time-to-diagnosis, a 37% reduction in out-patient visits, and a 35% reduction in the use of bed nights for neonatal care. There were no serious adverse events in women whose care was guided by PlGF testing compared with cases of cerebrovascular stroke, eclamptic fits, and myocardial infarction in women who received usual care.

The evidence in support of PlGF testing is strong and of high quality. We support APEC's campaign for PlGF testing to be made available across the United Kingdom.

Roche

NICE has recommended blood tests for pre-eclampsia. One of them is the Elecsys® sFlt-1/PlGF ratio test, used in combination with standard clinical practice, enabling clinicians to help rule out pre-eclampsia.

NHS England has assigned these tests as rapid uptake products, however they are not available to all expectant mothers. We would like to see the Royal College of Obstetrics and Gynaecology giving clear recommendations to its members to use the latest testing methods with appropriate populations, and that they make patients aware of their availability and importance.

Our ask is to see the widespread adoption of these tests in England, and their introduction in Wales and Scotland.

World Pre-eclampsia Day – May 22nd

- World Pre-eclampsia Day is recognised on May 22nd every year.
- Action on Pre-eclampsia are calling on the Government to recognise this day
- It is recognised by over 30 organisations worldwide including APEC, Save The Children, APEC Ghana, Pre-eclampsia Foundation (USA), USAID, Fetal Medicine Foundation and the European Foundation for the Care of Newborn Infants.
- It has support from the International Society for the Study of Hypertension in Pregnancy and is managed through Ending Eclampsia, a US based NGO.
- The organisations join together to highlight the common occurrence and devastating impact of preeclampsia, eclampsia, and other hypertensive disorders of pregnancy (HDPs).
- It supports all efforts that:
    - ✓ Call upon governments and health systems to recognize the importance of detecting and diagnosing risk factors, and preventing and treating the HDPs and related NCDs;
    - ✓ Encourage additional research funding into preeclampsia and related disorders;
    - ✓ Prioritize patient and community education and treatment for these disorders;
    - ✓ Prioritize education, training, and access to medical resources for healthcare providers;
    - ✓ Address prevention through a better understanding of the causes and through access to appropriate, safe, and effective treatments;
    - ✓ Encourage collaboration and partnerships between public and private sector organizations to support and advance these goals.

Case Study

Rob and Kate Crussell suffered the loss of their son Theo in 2015. This was a speech Rob made to a meeting in the House of Commons on 13th November last year

August 2015 should have been the best week of my life but sadly ended up being the worst, as we were due to meet our new son or daughter immanently. On Monday 3rd of August my wife had a routine midwife appointment and she had a small amount of protein in her urine but was told this was ok.

On the Wednesday afternoon Kate had a headache she couldn't shift and felt the baby's movement change, we decided to have dinner to see if food or a cold drink would make baby move more.

Later on that evening we decided to go to the labour ward and the midwife saw Kate's blood pressure of 216/110. Once the doctor saw Kate's blood pressure, she said the baby needs to be delivered tonight. The doctors think Kate was minutes away from having fits or even a stroke that's when the atmosphere changed in the room. Within minutes there were doctors and midwives all over Kate getting her ready for theatre and just as quickly she was off. I was just left in the room on my own it was a very scary and lonely time for me as it all happened so fast, I didn't really understand what had happened.

After Theo was born the team worked to resuscitate Theo for 35 mins and they finally got a heartbeat,

Once they found a heartbeat he was whisked off to the Neonatal ward. As Theo had stopped breathing for such a long time he suffered massive brain injuries and we were told he probably wouldn't survive,

If he had lived then he would be severely brain damaged. They actually discovered that he could breathe by himself when he came down to the ward where Kate met him and have a cuddle at about 5 hours old.

He managed to live for 44 beautiful hours, where we got the opportunity to change him, bathe him and see his ridiculously long toes and to spend some time with immediate family meeting and saying goodbye to our baby. He died in Kates arms on the Friday night with just me and Kate in the room I will never forget that moment.

Kate stayed in hospital for a week after Theo was born as she was so poorly, luckily, I was allowed to stay with her all the time.

Kate had 24 hour midwife care for some of this time and was on a magnesium sulphate drip for the prevention of seizures. Her blood pressure was difficult to control and she ended leaving hospital taking three different types of blood pressure medication to control it, having to take medication every three hours until gradually it could be reduced as my blood pressure started to come down.

Going through this type trauma has left Kate feeling extremely anxious, still even to this day.

It breaks my heart that up until this point Theo was a healthy baby boy and it was just this horrible disease that killed him. Kate's blood pressure had been normal on the Monday when it was checked and its scary to think that something like this can literally spike within days. We were told that Kate was lucky to be alive, if Kate hadn't gone in that night she would have died in her sleep - this is something that changes you as a person and something that even today She really struggles with as do I.

To date me and my wife have raised over £50,000 for 2 charities and our local hospital including over £23,000 for APEC. I had never heard of Pre-eclampsia before Theo so the awareness they raise is very important to saving not only babies but mothers lives too."

Further information

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