FOR IN-HOME DETECTION OF AMNIOTIC FLUID

FOREWORD

PREGNANCY is punctuated by questions, especially for first time expectant mothers. After all, how can a mother-to-be tell what is 'normal' when she has never been through this incredible physical and emotional journey before?

During pregnancy, women are reminded of the importance of seeking medical advice if they have questions or are unsure about physical changes, so it is crucial to find the right balance between caution and the need to seek urgent advice.

One challenge that many expectant mothers experience is urinary incontinence and wetness. Research by the Chartered Society of Physiotherapy and Royal College of Midwives confirms that one in three women (34%) experiences urinary incontinence during pregnancy. While this can be embarrassing and uncomfortable, there is no danger for either mother or baby.[1]

However, a 'leak' can be a sign of a premature rupture of the amniotic sac, which presents a risk to both mother and child, and may require urgent medical attention. Estimates vary, and are complicated by differing definitions of PROM in the UK and US, but as many as one in ten pregnancies is complicated by PROM — premature rupture of the membranes[2] — and in three out of five cases women go into labour within 24 hours.[3] But as there is no way of predicting who will go into labour, it is crucial to confirm whether the dampness is amniotic fluid, or not.

Now there is a simple DIY diagnostic at home test which offers evidence-based answers for amniotic leaks - **AmnioSense™**.

This report, from the PROM Education and Advisory Panel explores the risks, research and realities surrounding the problem of PROM and prolonged PROM, and reveals how **AmnioSense** provides the clear guidance women need when they suspect a rupture or their labour is on the way.

As Baroness Julia Cumberlege, chair of the recent National Maternity Review, pointed out: "Women have made it abundantly clear to us that they want to be in control of their care, in partnership with their healthcare professionals."[4]

Community Midwife, Emma Herbert says: "**AmnioSense** gives women control by providing a simple, effective, at-home test which allows them to differentiate between a pregnancy anxiety and a complication where medical review is needed urgently."

"Increasing awareness of this proven diagnostic test, **AmnioSense**, could help prevent unnecessary attendances at over-stretched maternity assessment centres and Accident and Emergency Departments."

"I have been surprised at how many of my lower-risk ladies who already have children say they really value being able to confirm whether or not their waters have broken. It allows them time to call a family member or friend to provide child-care and gives them the confidence to avoid coming into the maternity unit when they don't need to."

SAFETY SAC

The amniotic sac is a double membrane. It is filled with fluid, which begins forming within days of conception and provides protection and support throughout the pregnancy, usually until the ‘waters break,’ the beginning of the baby’s delivery.

At its peak capacity, which is around week 34 to 36, the amniotic sac will hold around two pints of clear, slightly yellow, fluid. Having too much, or too little fluid can lead to complications because the amniotic fluid and sac play a number of important roles.

This protective cocoon provides a buffer from bumps and injuries, ensures the umbilical cord is never compressed, which would reduce the developing baby’s oxygen supply. It also maintains a constant temperature within the womb.

As the fetus grows, it ‘breathes in’, swallows and excretes amniotic fluid and this aids development of a healthy respiratory and digestive system.[5] Amniotic fluid provides the space and support for the baby to move around, which is important for developing muscles and bones.[6,7]

Cells from the fetus accumulate in the fluid, so a small sample of amniotic fluid can be used to check for signs of any chromosomal or genetic abnormalities. This is carried out between the 11th and 14th weeks while amniocentesis, or ‘amnio’ as it is sometimes called, is usually carried out between weeks 15 and 20 of the pregnancy. Both carry a small risk of complications, including a premature rupture of the amniotic sac and miscarriage.

FACTS

- Insufficient amniotic fluid, known as oligohydramnios, occur in around 4% of pregnancies.[8]
- Dehydration, diabetes, placental problems and damage to the amniotic sac can all lead to insufficient fluid.[9]
- Excess fluid or polyhydramnios, is thought to occu in around 1% of pregnancies[10] and one in five cases are associated with a congenital abnormality.
- Women with diabetes, or who are carrying more than one baby are at greater risk of having excess amniotic fluid.[11]

THE CHALLENGE OF RUPTURES

The terminology used to describe rupture of the amniotic sac can vary. In the UK, we use:

- **SROM** which describes spontaneous rupture of membranes, when the waters break naturally sometime after week 37 and the woman goes into labour.
- **PROM** is premature rupture of membranes, which is a rupture before 37 weeks which is followed by spontaneous labour. These women need to be identified to ensure those who do not go into labour receive appropriate treatment. In the US, this term also includes P-PROM.
- **P-PROM** is pre-term premature rupture of membranes. In this case the membranes rupture before 37 weeks but the mother does not go into labour within 18 to 24 hours. The challenge for doctors is that this is, by definition often a diagnosis that can only be made retrospectively.

It is crucial to identify women who may not go into labour and become P-PROM because a third of women (36%) who experience a confirmed P-PROM have an infection inside the womb. In some cases, there may be warning signs, such as raised temperature or an unpleasant vaginal discharge. In most cases the infection is subclinical, which means there are no obvious symptoms until amniotic fluid begins to leak out, or the waters break completely.[12]

Having too much amniotic fluid, or carrying more than one baby, can over-stretch the amniotic sac and cause an early rupture. Women who have experienced PROM during a previous pregnancy are at increased risk of it happening again.[13]

Women who have undergone cervical surgery — such as a cone biopsy or laser treatment following an abnormal smear test — or those who just happen to have been born with a shorter cervix are also at greater risk.[14,15,16] Around 31,800 cases of in situ cervical carcinoma are picked up every year in the UK[17] and two out of five of these women will undergo surgical resection as part of their treatment.[18]

Some placental problems can lead to a rupture and tests such as amniocentesis and CVS also carry a small risk.

Diabetes is a danger because it can lead to excess amniotic fluid and over-stretching of the membranes. GP Dr Paul Stillman notes: “We are seeing a number of women who already have diabetes when they conceive. More and more are being diagnosed with the condition during pregnancy.”[19]

“But diabetes is not good news on so many levels. It involves many extra checks and monitoring. In addition, there is a real concern that health professionals don’t always have the time or resources to flag up the risk of PROM.”

The National Institute for Health and Care Excellence (NICE) estimates that one in 20 women (5%) who gives birth in England and Wales has diabetes, and almost nine out of ten (87.5%) of them are diagnosed during the pregnancy.

Being overweight increases the danger too. A study published in the Journal of the American Medical Association, looked at birth records for more than 1.5million women. This research trial found the chances of going into early labour with problems such as a premature rupture, rose in line with increases in the mother’s Body Mass Index.

A BMI of between 25 and 30 was associated with a 21% increase in premature rupture; a BMI of 30 to under 35 upped the odds by 27%; 35 to less than 40 raised the threat by 35% and a BMI of more than 40% increased the risk by 52%.[20]

The nutrition issue

Poor nutrition and low haemoglobin — which is caused by iron deficiency — have been linked to PROM.[21] This is worrying as low iron intakes are common among women in the UK. The latest National Diet and Nutrition Survey confirms that more than a quarter of women aged 19 to 64 (27%) and almost half the girls aged 11 to 18 (48%), are failing to meet the minimum intakes of iron needed for good health.[22]

While iron supplements are often prescribed during pregnancy, they are poorly absorbed and side effects are so common. Research suggests that two out of five women ignore advice to take them regularly.[23] Some researchers believe that having low levels of vitamins C and E increases the risk of early rupture.[24]

Smoking

Smoking is another risk factor, particularly early in the pregnancy.[25] A large Canadian study, which analysed data from 17,961 births, found that smoking more than 10 cigarettes a day significantly increases the danger of a woman's waters breaking too soon.

Endometriosis

Endometriosis, a gynaecological condition characterised by heavy periods and endometrial cells growing outside the womb, has also been shown to increase the risk of a premature rupture. Although it affects one in 10 women of child-bearing age, endometriosis is difficult to detect and on average women have to wait 7.5 years from the time they seek help to a confirmed diagnosis.[26,27]

Asherman Syndrome

Asherman Syndrome, which is characterised by adhesions and scarring of the womb lining is also associated with an increased risk of PROM. It is not clear how many women may be affected by Asherman's, but having a previous miscarriage or dilation and curetfage (D&C) increases the risk.[28]

TIMING AND TREATMENT

Membranes can rupture at any stage of the pregnancy. The treatment options and outcomes depend on the baby's development, the extent and position of the tear and — most importantly — how quickly the mother receives medical care or goes into labour.

Emma Herbert notes: "Many risk factors and variables will influence outcomes, but one thing is a constant: if a leak of amniotic fluid is suspected before 37 weeks, it must be investigated at once because both the mother and child may need immediate and expert attention."

NICE National Institute for Health and Care Excellence

"The early detection of leaking amniotic fluid, and appropriate management, may lead to a reduction in maternal and neonatal morbidity."

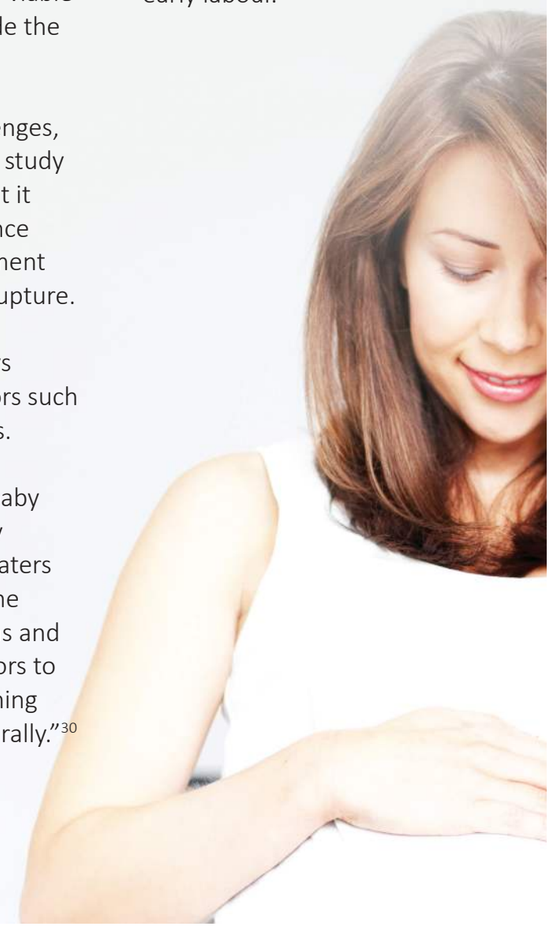
Issues at 20 weeks

Research at Newcastle University confirms that advances in care mean there is now very little difference in survival rates of a little one when there is a rupture between 20 and 24 weeks. This is compared to those occurring after week 24 — which is, by law, the line between a fetus and a baby and is widely considered the threshold for the baby to be 'viable' and be able to survive outside the womb.[29]

Commenting on these challenges, Dr Paul Stillman notes: "This study is incredibly encouraging, but it also underlines the importance of rapid diagnosis and treatment when there is a premature rupture. Modern medicine can work miracles, but it cannot always overcome confounding factors such as infection and fetal distress.

"The chances of a preterm baby surviving improve with every additional week and if the waters break at 34 weeks or later, the Royal College of Obstetricians and Gynaecologists advises doctors to induce the delivery — assuming contractions don't start naturally."[30]

Sometimes women who have had surgery to their cervix, or there is some underlying weakness, have a cerclage, or cervical stitch, to prevent it becoming dilated too soon. If there is any suspicion that amniotic fluid is leaking it is imperative that they get urgent medical attention as the stitch could introduce infection, or cause problems if they go into early labour.



Antibiotics

Antiobiotics are prescribed as soon as a leak is detected because one in four women carries group B Strep. These harmless bacteria may increase the risk of a rupture and can invade the amniotic sac and infect the baby if there is a leak. This can lead to a number of problems including heart and breathing issues, pneumonia and meningitis.[31]

Study facts

Twenty-two trials involving more than 6,000 women who experienced PROM, confirm that giving prophylactic antibiotics almost halves the risk of infection and significantly reduces the risk of infants being born within the following 48 hours.[32]

Steroids

Steroids are given to speed up the development of the baby's lungs, which are the last organ to mature. The alveoli, tiny sacs at the ends of the respiratory tree which allow oxygen to pass into the bloodstream and carbon dioxide out, do not normally begin forming until around week 26 and it is a further 10 weeks before the surfactant system (a fatty coating which prevents the lungs collapsing during outward breaths) is fully formed.[33]

Clinical data

Studies involving more than 1,400 women given steroids following a premature rupture confirm the medication almost halve the chances of the baby suffering respiratory distress (44% reduction) or a brain haemorrhage (53% reduction).[34]

'LEAKS' – DID YOU KNOW?

Emma Herbert says: "When the amniotic sac ruptures with the classic 'gush of fluid' there is absolutely no mistaking what has happened, but it is much more difficult to identify a small rupture which releases tiny amounts of amniotic fluid."

"It is quite common for women to notice increased wetness during pregnancy, and in most cases this is nothing more serious than a leak of urine. Many women suffer mild incontinence as their baby-bump weighs down on their bladder and pregnancy hormones relax the pelvic-floor muscles which would normally prevent any urine escaping."

It's also not unusual for hormonal changes during pregnancy to increase the amount of mucus, moisture and discharge in the vagina. Mild infections such as thrush or bacterial vaginosis may also mimic PROM.[35]

SECTION 4

TEST THAT MAKES SENSE

AmnioSense is an evidence based home test which has been proven to be as accurate as hospital-based tests when compared to the most common tests performed in hospital; sterile speculum examination, microscopic ferning test and pH paper test. It helps identify the cause of any unexpected leaks. In two out of five cases, it also enables an accurate diagnosis without the need for a physical examination of the cervix using a speculum.[36]

Unlike hospital based tests, **AmnioSense** allows continuous monitoring and detects minute leaks. **AmnioSense** is so sensitive it reacts to as little as 100 microliters of amniotic fluid, the equivalent of two drops.[37]

AmnioSense looks like an ordinary panty-liner. However it includes a polymer strip which turns blue-green when it comes into contact with moisture with a pH — a measure of alkalinity or acidity — of more than 6.5. Amniotic fluid has a pH of 6.7 or more while normal vaginal secretion ranges from 3.5 to 4.5.

The pH of urine can vary from 4.0 to 8,[38] but it also contains ammonia. As a result, **AmnioSense** includes reagents which react differently to ammonia. This helps eliminate any false positives caused by incontinence. In some cases, if the leak is urine, the pad will change colour immediately, but then fade within 10 minutes. The test area will remain a blue-green colour for at least two hours when the reaction has been triggered by amniotic fluid.

Commenting on **AmnioSense**, Emma Herbert notes: “A great advantage with **AmnioSense** is that the panty-liner can be worn for up to 12 hours, making it very efficient at detecting small, slow leaks of amniotic fluid and hind leaks, which are notoriously difficult to spot. As the results are stable for at least two hours there is often time for the woman to get to her midwife or maternity unit and show them the results.”

YELLOW
Indicates probable urine leakage

BLUE
Indicates probable amniotic fluid leakage

Clinical evidence

Clinical trials in both the laboratory and real-world setting, and independent evaluation by NICE, have all confirmed the accuracy and effectiveness of **AmnioSense**.

A simple proof-of-principal test published in the International Journal of Clinical Medicine used samples taken from 50 women, who were between 16 and 23 weeks pregnant, for amniocentesis tests. **AmnioSense** positively identified the fluid with 100% accuracy, and the results could be read for up to 12 hours.[39]

A further study involving 339 women attending hospital with unexplained vaginal wetness found that **AmnioSense** correctly detected 154 of the 161 cases where a leak of amniotic fluid was confirmed.[40] This study also demonstrated the results are clear enough to be interpreted accurately by pregnant women, with 97% alignment between subjects and healthcare professionals.

The trial reported in the American Journal of Perinatology, described **AmnioSense** as a "Highly sensitive, non-intrusive method to detect the presence of amniotic fluid."

The researchers pointed out: "False-positive results may occur in women with bacterial vaginosis or trichomonas vaginitis." Another trial investigated the use of **AmnioSense** with 157 women attending the antenatal unit at St Thomas' Hospital in London with a suspected leak of amniotic fluid. Some had been referred to the unit by their GP or midwife, while some had been so concerned they went straight to the hospital.[41]

In all, 139 were eligible for the trial and were asked to wear the **AmnioSense** panty-liner for 20 minutes, or until they were aware of any dampness. After 10 minutes, the liner was checked by a midwife, who recorded the results. A second midwife, who was given no information about the findings, then carried out tests involving internal examination using a speculum to confirm whether or not there was a leak.

Comparisons confirmed that AmnioSense detected 98% of leaks caused by amniotic fluid and 67% were confirmed as not caused by amniotic fluid. Two out of five (38%) could have been diagnosed without the need for invasive investigation using a speculum — which itself can increase the risk of infection. While there were some false positives, a quarter of these were linked to the presence of bacteria or fungal infections, including candida, Group B Strep and staphyolococcus aureus.

The study, published in the Journal of Obstetrics and Gynaecology concluded: "If used in clinical practice, the reduction in the number of speculum examinations will substantially benefit women and service providers. All women with a positive test result require further investigation."

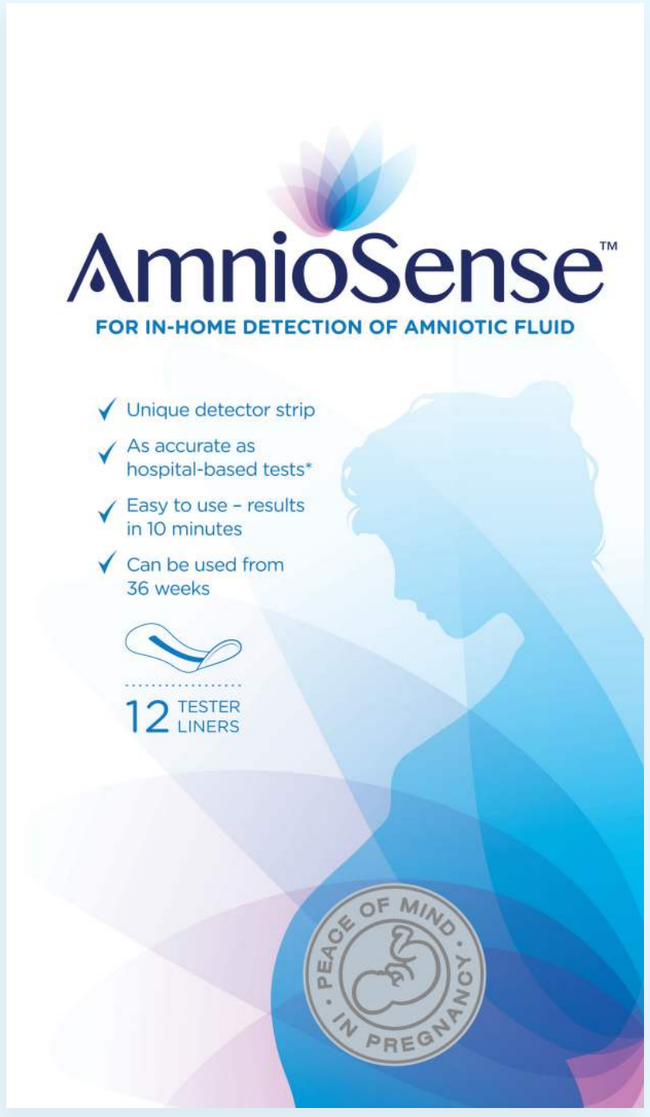
A further trial compared results from 103 women attending the labour and delivery ward of an Israeli hospital. A third of trialists had suspected leaks, a third with confirmed leaks and a third, with no symptoms, who acted as a control group.[42]

Of the 34 women with suspected leaks, **AmnioSense** panty-liner correctly identified the presence of amniotic fluid in 10 cases. Follow-up checks confirmed this result was 100% accurate and every case of rupture was identified. Of the six women who tested positive, four were subsequently found to have bacterial infections and the other two were diagnosed with PROM a few hours after the initial negative result.

The investigators concluded that **AmnioSense** is: "A highly sensitive, non-intrusive method for use in ruling out the possibility of PROM. It is also capable of differentiating PROM from urinary incontinence or vulvo-vaginal candidiasis, thereby avoiding misdiagnosis, unnecessary treatment, and interventions, which reduces patient anxiety and lowers costs."

Dr Paul Stillman adds: "The fact that it also picked up issues with the so-called 'false positive' results suggest that the **AmnioSense** is actually better at picking up small leaks and other problems than the more invasive tests which are usually carried out."

"This study undoubtedly reinforces the case for using **AmnioSense** as a frontline check as this would eliminate the need for more uncomfortable investigations."



HOW TO USE AmnioSense

"The simplicity and comfort of **AmnioSense** are two of its greatest strengths," says Emma Hebert.

"A lot of women find it more comfortable to wear a panty-liner during pregnancy, but this liner gives the added reassurance of warning when a leak warrants further investigation."

The liners should always be kept in a dry place to avoid any contamination, and should not be opened until they are going to be used. It should then be worn for up to 12 hours or until wetness is felt. However, it should not be used within 12 hours of having intercourse as the presence of semen is likely to trigger a false positive result. Douching, which is also not medically recommended, may also lead to a false positive result.

If there is no colour change, the moisture is harmless vaginal secretions or urine. However, if the fluid has a higher pH than 6.5, the liner will turn blue-green. If the fluid is urine, special reagents in the test strip will prevent stains or make the colour fade away inside 10 minutes. If it is amniotic fluid the strip will remain blue-green for at least two hours. It is essential to wait 10 minutes before assessing the colour change. Urine with a very high pH (above 7) may also produce a false positive.

LAST WORD

Emma Herbert says: “The development of **AmnioSense** is great news. The published, clinical evidence behind **AmnioSense** is very impressive and the product has the proven ability to help identify the cause of any unexpected leaks rapidly.”

“Minor leaks and dampness are commonplace during pregnancy. In most cases, a leak presents no threat to either the mother or the baby. However, it can be difficult to tell the difference between a harmless dribble of urine or vaginal discharge and the potential medical emergency of a leak in the amniotic sac.”

The use of **AmnioSense** could also save the NHS money. A NICE review pointed out, a single visit to an antenatal unit costs £147 and research shows that 38% of women who used **AmnioSense** did not have to attend because they were able to confirm leaks were harmless.[43]

Dr Paul Stillman adds: “There are around 695,000 live births in England and Wales every year,[44] and around a third of those will notice some sort of leak[45] — which adds up to a potential saving of £880,000,[46] not to mention untold concern.”

In summary, Emma Herbert notes: “The feedback I have had from women who have tried **AmnioSense** is that it can take some of the worry out of pregnancy by providing a simple and accurate home test to confirm whether or not their waters have broken. **AmnioSense** also provided them with peace of mind.”

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AmnioSense™