Important Things to Consider If You're Pregnant

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Overview:

Placenta accreta spectrum disorder (PAS), also known as abnormally invasive placenta (AIP), depicts a clinical situation in which the placenta fails to detach spontaneously after delivery and has to be forcibly remove with the risk of having massive and potentially life threatening bleeding, or hemorrhage. Placenta accreta, in recent years, has been an increasingly more common condition among pregnant people. To be exact, the rates in which placenta accreta occur had quadrupled since the 1980s, which is unsurprising due to the increasing usage of the Cesarean section as the preferred surgical procedure of delivering babies out of the womb. Currently about 1 in 500 pregnancies will be involved with placenta accreta.

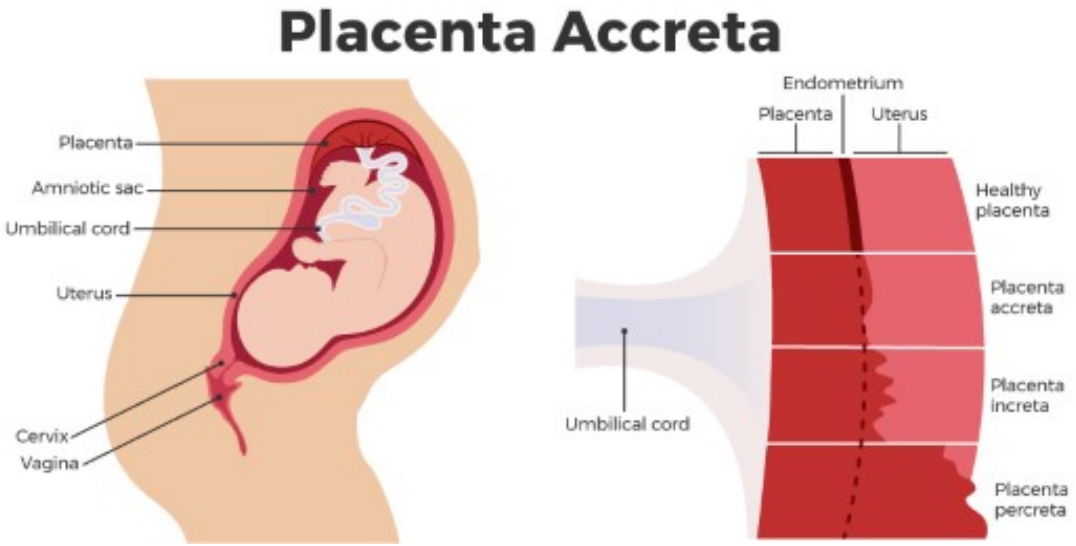
Placenta accreta possesses a significantly high morbidity rate due to the failure by the post-delivery placenta to separate from the uterus. This condition is caused by the placenta growing too deeply into the uterine wall and fails to detach with it. The placenta accreta spectrum consists of placenta accreta, placenta increta, and placenta percreta in increasing severity. The majority (75-78%) of the confirmed diagnosis was revealed to be placenta accreta, placenta increta and percreta still made up about 17% and 5%, respectively.

There are a lot of complications and symptoms that can be associated with placenta accreta, including infection, abnormal placental separation during delivery, postpartum hemorrhage, disseminated intravascular coagulation, potential emergency hysterectomy, maternal death, and premature labor. The most important risk factors for PAS are placenta previa (when the placenta implants low and overlays the cervix) and prior cesarean deliveries. There are multiple clinical screening diagnostics for placenta accreta, with the main ones being ultrasonography and magnetic resonance imaging. Grayscale ultrasonography is sensitive (77–87%) and specific (96–98%) for the diagnosis of placenta accreta. Ultrasonography is usually the most common prescribed and preferred method among doctors due to its accuracy and availability. The price range for obtaining an ultrasound is usually between $155 to $760. Magnetic resonance imaging, or MRI, may be helpful when the ultrasonography results are unclear or a suspicion of posterior placenta accreta. MRI works by employing strong magnetic fields and radio waves to obtain high accuracy images of internal organs and tissues. Because MRIs are more expensive, ranging from $1584 to $7600, they are less frequently ordered after a patient has had an indeterminate ultrasound result.

Placenta Accreta Spectrum:

Placenta Accreta Spectrum (PAS), is when the placenta is attached to the wall of the uterus and does not leave the uterus after birth. In a normal pregnancy, the placenta will exit the body after delivery. With PAS, the placenta will remain firmly attached to the uterus.

There are three types of PAS. Placenta accreta occurs when the placenta is attached to the wall of the uterus but does not go through the wall of the uterus. This is also the most common type of PAS. Placenta increta is when the placenta is attached to the muscle of the uterus but still does not pass through the wall. Placenta percreta is the most severe and the rarest of the three. The placenta goes through the uterine wall and on to another organ, like the bladder. PAS can result in premature birth along with extreme vaginal bleeding (hemorrhage) after delivery. The bleeding can be life-threatening as it prevents blood from clotting normally. These issues can also lead to lung and kidney failure.

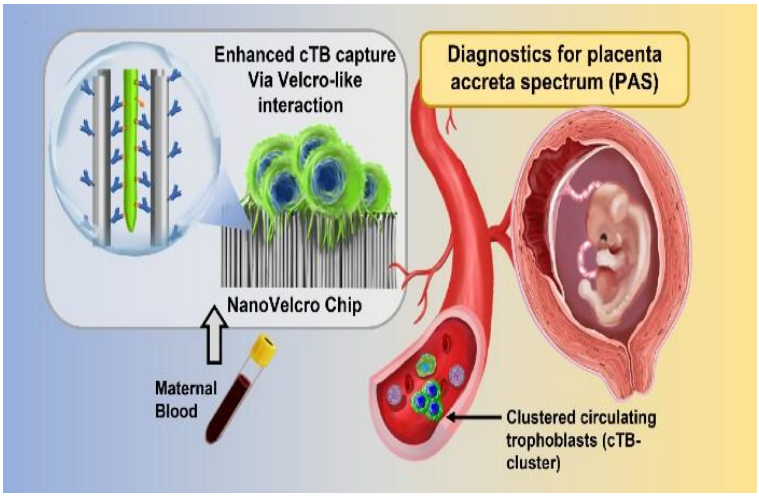


Trophoblast:

Trophoblasts are layers of cells that provide nutrients to the embryo and then attach the embryo to the wall of the uterus, which later on develops into a large part of the placenta. Trophoblasts form during the first stage of pregnancy, and there are two different layers of trophoblasts: cytotrophoblasts and syncytiotrophoblasts. Cytotrophoblasts are the inner layer of the trophoblast that resides under the syncytiotrophoblast. The syncytiotrophoblast is made up of cytotrophoblast fused together. It will invade the uterine wall, which begins the exchangement of nutrients and wastes between the mother and the embryo.

A successful pregnancy depends on the trophoblast invading the pregnant individual. The trophoblast invasion ensures the attachment of pregnant individuals to the uterus, this secures a surplus amount of oxygen and nutrients to the fetus. Failure of trophoblast invasions can lead to preeclampsia, which is one of the leading causes in maternal death.

Circulating trophoblasts (cTBs) are placenta based trophoblasts that are shed into a pregnant individual's maternal circulation during placenta development and implantation. cTBs can be used as an alternative form of genetic testing and prenatal diagnosis, but its main purpose is to migrate and invade the maternal interface for normal implantation and placentation. However, if a dysfunction with cTBs occurs, clusters and abnormal invasions may form, potentially leading to placenta accreta spectrum and/or miscarriage. These clusters of cTBs can be detected and caught using NanoVelcro Chips. Fluorescent microscopes are used to differentiate cTBs from white blood cells.



Introduction to Non-invasive Prenatal Testing (NIPT):

Non-invasive prenatal testing (NIPT) is a relatively new method of screening for fetal abnormalities during pregnancy. Unlike invasive prenatal tests that require the insertion of needles or probes into the uterus, this method of testing does not cause harm to the fetus since it only requires a small sample of maternal blood. Specifically, NIPT uses cell-free fetal DNA (cffDNA) found in maternal plasma to test for aneuploidy and single-gene disorders such as Down syndrome, Turner syndrome, cystic fibrosis, and Huntington's disease.

The two most commonly used NIPT methods in the United States are quantitative “counting” using targeted parallel sequencing and single-nucleotide polymorphism (SNP) that identifies maternal and fetal allele distributions (it should be noted that the SNP-based method cannot be used when there is a possibility of external DNA from a third party, such as an egg donor). As mentioned above, NIPT requires the presence of cffDNA (small fragments of DNA released by placental cells when they undergo apoptosis) in maternal plasma, which is then amplified using polymerase chain reaction (PCR) techniques. In the counting method, next-generation sequencing is performed to align the DNA fragments, allowing for the origin chromosome to be identified from a human reference. The DNA fragments are then counted and compared to the amount of DNA present in the origin chromosome, and if there are more DNA fragments, fetal trisomy may be more likely to occur. In the SNP-based method, maternal cells are separated from the blood sample, and the SNPs from these maternal cells are then compared to the SNPs from a cffDNA/maternal mixture. Aneuploidy is indicated when the ratio or pattern of the differing maternal SNPs and cffDNA SNPs changes.

NIPT has been commercially available since 2011 and costs around $600 to $800 to perform in the United States. While expensive, it can be done starting from the ninth or tenth week of pregnancy and avoids the risk of miscarriage. It is also both highly sensitive (90 to 99%) and highly specific (99% to 100%), but it is important to note that NIPT is not a diagnostic test; it does not have the accuracy to diagnose any abnormalities, but it can determine the risk level for said abnormality. If a high-risk result is determined through NIPT, patients may choose to continue with invasive testing.

Nano-Velcro Chip:

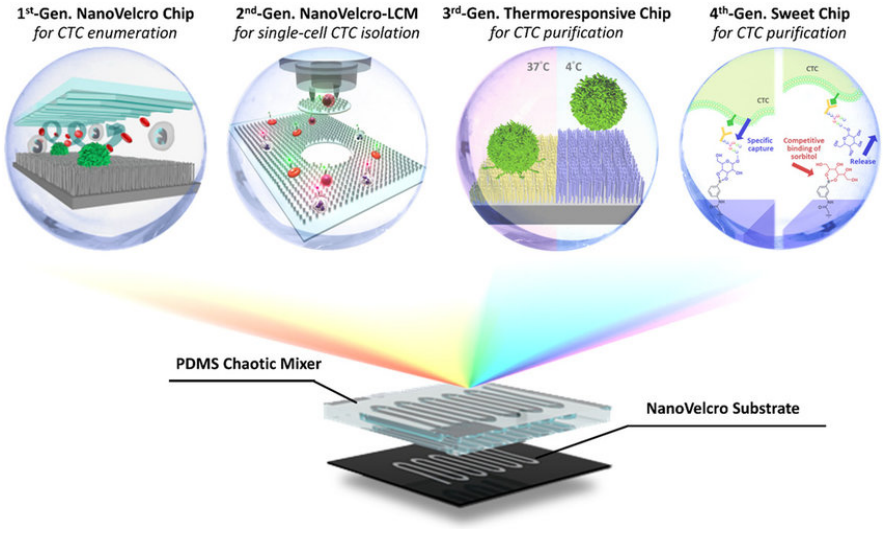
Although many individuals suffering from medical disorders and conditions have choices for intervention, many miss this chance. Medical screening for critical disorders often requires lengthy procedures and high costs. As a result, many conditions can go unnoticed. This is especially threatening to individuals suffering from placenta accreta spectrum, a life-threatening condition occurring after childbirth.

However, a recent advancement in medicine allows for more accessible screening to prevent fatalities from PAS. Originally developed to aid doctors in the detection of circulating tumor cells (CTCs), the NanoVelcro Chip is now able to detect placenta cells within blood samples of pregnant individuals.

The NanoVelcro Chip, a lot like the velcro tapes used in our lives daily, is similar in size to a postage stamp. Blood samples are run through tiny nanowires 1,000 times thinner than a human hair. These nanowires then capture the Circulating Trophoblasts (cTBs) in the patient's blood. As a sample of blood is run through a NanoVelcro Chip, cTBs will become trapped in the small nanowires across the chip. As the number of cTBs increases, so will the amount trapped.

Circulating trophoblasts that circulate the patient's blood when PAS is present can exist as single cTBs or cTB clusters. When these trophoblasts are captured by the NanoVelcro chip it is then determined if the patient has PAS. Through studies, it is found that blood samples from women with normal placenta previa contain no clusters of cTBs. In other words, the amount of cTBs present in a patient's blood determines their chances of having PAS.

Not only doNanoVelcro Chips provide patients with PAS with an inexpensive and widely available option, it is also a much easier and faster alternative besides ultrasonography and MRI. The NanoVelcro Chip is able to detect PAS as early as the first trimester of pregnancies while ultrasonography and MRI are only effective in the third trimester. Early detection of PAS decreases the risk of increased damage to the placenta. Diagnosed patients can be treated quickly without the placenta accreta advancing to become increta or percreta, avoiding risk of death, miscarriage, and other symptoms.



How we can help:

The AEC PAS (Placenta Accreta Spectrum) is a program developed for helping pregnant individuals recognize the symptoms of placenta accreta before it develops into something worse, such as increta or Percreta. Unfortunately, many pregnant people aren't recognized to have placenta accreta until it's too late in the stages to do anything, and we hope you won't be another example of that. NanoVelcro circulating trophoblasts (cTB) Assay is a non-invasive form of testing, only needing a sample of blood (as opposed to painful and invasive surgery). With your help, we can help you figure out if your placenta is in dire condition early on with a quick and effective method. Your blood sample is collected and loaded into the NanoVelcro Chip, which is especially designed to trap certain cells including circulating trophoblasts. UCLA offers safe and non-invasive clinical trials available to the public.

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