

## Clinical References

Following is a list of AFL™ (Amniotic Fluid Lactate) related publications or publications related to the subject. The publications are listed in chronological order.

### AFL™ related publications

- **Association Between Adverse Neonatal Outcome and Lactate Concentration in Amniotic Fluid.**

*Eva Wiberg-Itzel, Helena Akerud, Ellika Andolf, Lena Hellström-Westas, Birger Winbladh and Ulla-Britt Wennerholm*  
(*Obstet Gynecol* 2011;118:135–42)

RESULTS: .....If lactate in amniotic fluid was greater than 10.1 mmol/L and bradycardia was seen together, the risk of delivering a neonate with an adverse neonatal outcome was increased 11-fold.....

CONCLUSION: High lactate concentration in amniotic fluid and fetal bradycardia during the last 30 minutes before delivery indicate an increased risk of adverse neonatal outcome at delivery.

- **Lactate concentration in amniotic fluid: a good predictor of labor outcome.**

*Wiberg-Itzel E, Pettersson H, Andolf E, Hansson A, Winbladh B, Akerud H.*  
(*Eur J Obstet Gynecol Reprod Biol.* 2010 Sep;152(1):34-8. Epub 2010 Jun 9.)

OBJECTIVE: Previous publications have suggested that high levels of lactate in amniotic fluid (AF) correlate with dysfunctional labor. The aim of this study was to investigate whether lactate concentration in AF together with the partogram is a better predictor of operative intervention in dysfunctional labor than the partogram alone.

CONCLUSION: The partogram together with the concentration of lactate in AF is a better predictor of operative intervention in dysfunctional labor than the partogram alone.

- **Lactate distribution in culture medium of human myometrial biopsies incubated under different conditions.**

*Helena Åkerud, Gunnar Ronquist and Eva Wiberg-Itzel*

(*Am J Physiol Endocrinol Metab.* 2009 Dec;297(6):E1414-9. Epub 2009 Oct 13.)

The purpose of this study was to examine whether myometrial cells are involved in the production of lactate in amniotic fluid and whether there are differences in production and distribution of lactate in cells incubated under aerobic and anaerobic conditions.....

The presence of lactate carriers named monocarboxylate transporters 1 and 4 was verified. Myometrial cells produced lactate extracellularly, and the lactate carriers operated differently under anaerobic and aerobic conditions; while being mainly unidirectional under anaerobic conditions, they became bidirectional under aerobic conditions. Human myometrial cells produced and delivered lactate to the extracellular medium under both anaerobic and aerobic conditions. The delivery was mediated by lactate carriers.

- **Association between lactate concentration in amniotic fluid and dysfunctional labor.**

*Wiberg-Itzel E, Pettersson H, Cnattingius S, Nordström L.*

*(Acta Obstet Gynecol Scand. 2008 Aug 11:1-5.)*

OBJECTIVES: To assess whether there is an association between high lactate concentration in amniotic fluid (AF) and labor dystocia.

CONCLUSIONS: High lactate concentration ( $>$  or  $=10.1$ mmol/l) in at least two consecutive samples of AF collected during labor 60 minutes apart is strongly associated with dystocia. This method might be useful in clinical management to identify labor dystocia at an early stage of labor.

## Other related publications

- **Insights into the uterus.**

*Wray, S*

*(Exp Physiol 2007; 92; 621-631.)*

A better understanding of the mechanisms that generate and modulate uterine contractility is needed if progress is to be made in the prevention or treatment of problems in labour. Dysfunctional labour describes the condition when uterine contractility is too poor to dilate the cervix, and it is the leading cause of emergency Caesarean sections..... I present the evidence that acidification of the myometrium is correlated with dysfunctional labour and suggest the processes by which it is occurring. It is only by gaining a better understanding of uterine physiology and pathophysiology that progress will be made and research findings translated into clinical benefit for women and their families.

- **Dysfunctional labor and myometrial lactic acidosis.**

*Quenby, S., et al.,n*

*(Obstet Gynecol, 2004. 103(4): p. 718-23.)*

OBJECTIVE: Inefficient uterine contractions are the most common cause of poor progress in labor. The global increase in cesarean delivery rate is a cause of considerable concern, and the greatest reason for increase is the result of failure to progress in labor. Following in vitro studies that showed acidification could depress uterine contraction, we hypothesized that it could contribute to dysfunctional labors.

CONCLUSIONS: Myometrial lactic acidosis and a small decrease in  $O_2$  saturation may be contributing factors to dysfunctional labor. Our data may also account for the ineffectiveness in management of dysfunctional labor with oxytocin. Oxytocin with a background of lactate acidosis may not be successful.

- **Calcium signaling and uterine contractility.**

*Wray, S., et al.*

*(J Soc. Gynecol Investig, 2003. 10(5): p. 252-64.)*

Changes in  $Ca^{2+}$  signals within the myometrium have important functional consequences, as they determine contractility. We show that the basic phasic nature of uterine contractions, which is essential for successful labor, is critically dependent on  $Ca^{2+}$  influx through voltage-gated L-type  $Ca^{2+}$  channels, and hence in turn, on membrane potential. ...

- Low myometrial glycogen content compared with rectus muscle in term pregnant women before labor.**  
*Steingrimsdóttir T, Ronquist G, Ulmsten U, Waldenström A. (Gynecol Obstet Invest. 1999;47(3):166-71.)*  
 Glycogen, glucose, some nucleosides and purine base derivatives were determined in biopsies from 10 term pregnant women undergoing elective cesarean sections before labor.
- Hypoxia and smooth muscle function: key regulatory events during metabolic stress.**  
*Michael J Taggart and Susan Wray (J Physiol. 1998 June 1; 509(Pt 2): 315–325.)*  
 .....Hypoxic changes of plasma membrane channel activity contribute to reduced contractility..... .
- External alkalization decreases intracellular Ca<sup>++</sup> and spontaneous contractions in pregnant rat myometrium.**  
*Taggart MJ, Sheader EA, Walker SD, Naderali EK, Moore S, Wray S (Am J Obstet Gynecol. 1997 Oct;177(4):959-63.)*  
 CONCLUSIONS: Raised external pH reduces spontaneous contractions in the pregnant rat uterus, probably by an external effect on Ca<sup>++</sup> entry. This effect may contribute to uterine quiescence before term.
- Human uterine smooth muscle exhibits a very low phosphocreatine/ATP ratio as assessed by in vitro and in vivo measurements.**  
*Steingrimsdóttir T, Ericsson A, Franck A, Waldenström A, Ulmsten U, Ronquist G. (Eur J Clin Invest. 1997 Sep;27(9):743-9.)*  
 The purpose of the study was to investigate by in vitro and in vivo methods the phosphocreatine (PCr)/ ATP ratio as an expression of the energy metabolic state of human myometrium in comparison with striated skeletal muscle.
- Stimulus-dependent modulation of smooth muscle intracellular calcium and force by altered intracellular pH.**  
*Michael J. Taggart, Theodor Burdyga, Richard Heaton and Susan Wray (Pflugers Arch, 1996. 432(5): p. 803-11.)*  
 .....In the presence of carbachol, acidification transiently increased force and [Ca<sup>2+</sup>]<sub>i</sub>, followed by a reduction in both. It is concluded that changes in pH<sub>i</sub> act at more than one step in excitation-contraction coupling and that changes in [Ca<sup>2+</sup>]<sub>i</sub> can account for most of the changes in uterine force.
- Different energy metabolite pattern between uterine smooth muscle and striated rectus muscle in term pregnant women.**  
*Steingrimsdóttir T, Ronquist G, Ulmsten U, Waldenström A. (Eur J Obstet Gynecol Reprod Biol. 1995 Oct;62(2):241-5.)*  
 .....The results indicated that the pregnant uterine smooth muscle utilized glucose as the principal nutritive metabolite rather than lipids and that the anaerobic pathway of the glucose metabolism was more active in the myometrium compared with the striated rectus muscle. Also, it is suggested that glucose has a critical role as the principal fuel for ATP formation and the involvement of the adenylate kinase and 5'-nucleotidase reactions in any event of glucose shortage.

- **Simultaneous measurement of intracellular pH and contraction in uterine smooth muscle.**

*Michael Taggart and Susan Wray*

*(Pflugers Arch. 1993 Jun;423(5-6):527-9.)*

.....Alkalinization greatly increased the frequency of contractions, often accompanied by a small increase in their amplitude. Removal of base produced a rebound acidification which transiently abolished contractions. Direct acidification of the cytoplasm, by application of weak acid, also abolished contractions. However the alkalinization which accompanied removal of acid, produced variable effects on force.

- **Balance of amino acids in the pregnant human uterus at term.**

*Steingrimsdóttir T, Ronquist G, Ulmsten U.*

*(Eur J Obstet Gynecol Reprod Biol. 1993 Aug;50(3):197-202.)*

.....Generally the AV differences are negative, i.e. uterus at term releases amino acids in most cases. The human pregnant uterus at term is characterized by a release of amino acids rather than uptake. This indicates that they are in excess and are not needed in anabolic processes or as a fuel, even when the uterine tissue at term is supposed to be preparing for its grand performance, i.e. the delivery.

- **Energy economy in the pregnant human uterus at term: studies on arteriovenous differences in metabolites of carbohydrate, fat and nucleotides.**

*Steingrimsdóttir T, Ronquist G, Ulmsten U.*

*(Eur J Obstet Gynecol Reprod Biol. 1993 Oct 29;51(3):209-15.)*

.....A distinct uptake of glucose was a typical finding in the pregnant uterus as reflected by a positive difference. On the other hand, glycerol and FFA were released from the pregnant uterus. Similarly, a degradation of adenine-containing nucleotides seemed to be continuously ongoing in the pregnant uterus, since oxypurines displayed a negative difference as well.

- **Regional differences in energy charge of the pregnant human uterus regardless of functional status in comparison with the non-pregnant uterus.**

*Wedenberg K, Ronquist G, Waldenström A, Ulmsten U.*

*(Biochim Biophys Acta. 1991 Jun 17;1058(2):147-51.)*

.....It shows that energy charge (EC) varies in different regions of the uterus in that the isthmic part in pregnant women displays a higher EC than the fundus of the uterus. There were no intergroup differences between non-pregnant and term pregnant women, nor between those who were in active normal labour, dysfunctional labour or those who were not in labour at all. On the other hand, EC in uterine muscle of post-menopausal women showed a significantly lower EC value. Human uterus seems to manage its metabolic requirements under different functional conditions in spite of low ATP and EC values. This suggests that ATP occurs in sufficient amounts to pertinent enzyme reactions, especially ATPases, which means Km values adapted for this unusually low ATP concentration.

- **Low energy charge in human uterine muscle.**  
*Wedenberg K, Ronquist G, Waldenström A, Ulmsten U. (Biochim Biophys Acta. 1990 Jan 29;1033(1):31-4.)*  
.....The lactate content in uterine biopsies from pregnant patients was significantly higher than that found in biopsies from rectus muscle and from uterine tissue of non-pregnant patients, indicating an increased glycogenolysis in pregnant uterus.....