Diplomarbeit

Die Wertigkeit des Laktats im Rahmen des foetalen blood samplings

eingereicht von
Natalie Fischer
Matr.Nr.: 0311930

zur Erlangung des akademischen Grades

Doktorin der gesamten Heilkunde
(Dr. med. univ.)

an der
Medizinischen Universität Graz

ausgeführt an der
Universitätsklinik für Frauenheilkunde und Geburtshilfe

unter der Anleitung von
Ao.Univ.-Prof. Dr.med. Wolfgang Schoell

Graz, 14.Dezember 2009 Natalie Fischer

Eidesstattliche Erklärung

Ich erkläre ehrenwörtlich, dass ich die vorliegende Arbeit selbstständig und ohne fremde Hilfe verfasst habe, andere als die angegebenen Quellen nicht verwendet habe und die den benutzten Quellen wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe.

Graz, am ……. Natalie Fischer

An dieser Stelle möchte ich erwähnen, dass soweit in dieser Arbeit Personen- und Funktionsbezeichnungen nicht ausdrücklich in der weiblichen und männlichen Form genannt werden, die sprachlichen Bezeichnungen in der männlichen Form sinngemäß auch in der weiblichen Form zu verstehen sind.

Danksagung:

Ich möchte mich bei Prof. Dr. Wolfgang Schöll für die motivierende, inspirierende und engagierte Betreuung dieser Diplomarbeit ebenso bedanken wie dafür, dass er es mir ermöglicht hat Einsicht in seine Tätigkeit im Bereich der Gynäkologie und vor allem der Geburtshilfe zu nehmen.

Zu dem mit dieser Arbeit eng verbundenen, nahenden Studienende ist es mir ein Anliegen ein großes *„Dankeschön“* auszusprechen an

…meine Familie, die mich in meinem bisherigen Leben stets aufopfernd und geduldig unterstützt hat.

…meine Freunde, die helfen, inspirieren und herausfordern.

… und an DEN Schatz, der mein Leben erfüllt, schöner macht…mich vervollständigt.

Zusammenfassung:

Hintergrund: Seit 1962 hat sich die Technik der Mikroblutuntersuchung des Babys unter der Geburt routinemäßig im Geburtsablauf verankert. Zur Anwendung kommt diese Untersuchung im Falle einer pathologischen Cardiotokographie (CTG) - Kurve. Hierfür wird während der Geburt ca.100µl Blut aus dem sich im Geburtskanal befindlichen Kopf des Kindes entnommen und der aktuelle Säure-Basen Haushalt bestimmt. Folglich wird der pH-Wert und der Baseexcess für die Entscheidung des weitern Geburtsverlauf oder einer eventuellen Intervention berücksichtigt. Zusätzlich wird auch der Laktatwert erhoben, jedoch bei der Entscheidungsfindung über das Weiterverfahren nicht berücksichtigt. Es ist bekannt, dass ein erhöhter Laktatwert ein Zeichen für eine metabolische Azidose ist und auch bei hypoxischen Kindern nach der Geburt beobachtet werden kann.

Fragestellung: Inwieweit ist der Laktatwert, der unter der Geburt mittels Blutgasanalyse erhoben wird aussagekräftig für das fötale Outcome bzw. welche Laktatwerte zeigen im weiteren Verlauf eine kritische Situation des Kindes auf.

Methode: Eine retrospektive Studie, die die Protokolle von über 767 Geburten und die darin erhobenen Mikroblutuntersuchungen der Abteilung für Gynäkologie und Geburtshilfe am Universitätsklinikum Graz vom Jahr 2004- 2007, einbezieht. Es werden Laktatwert, pH und Baseexcess erhoben und mit dem fötalen Outcome, das durch den *„Apgar-score“* definiert wird verglichen.

Resultate: Es zeigte sich eine eindeutige indirekte Korrelation zwischen pH und Laktat. Weiters konnte eine indirekte Korrelation zwischen Laktatwert und Apgar 1, welcher als Variable für das fötale Outcome definiert wurde, nachgewiesen werden. Ein “zufriedenstellendes fötales Outcome” wurde im Vorhinein definiert als APGAR 1 > 7. Ein Cut – off - Wert, der dieses Vorhersage zufriedenstellend erlaubt, wurde statistisch als kleiner als 4.2 mmol/L ermittelt.

Schlussfolgerung: Der Laktatwert ist ein signifikanter Wert zur Beurteilung der derzeitigen fötalen Sauerstoffversorgung beziehungsweise des folgenden Outcomes. Als Grenzwert um dieses zu garantieren und eine eventuelle Intervention einzuleiten kann ein Laktatwert von kleiner als 4.2 mmol/L angegeben werden.

Abstract:

Background: Saling's technique of analyzing foetal scalp blood during delivery became a standard obstetric practice in monitoring neonates ever since it's first use in 1962. It is an examination in which a small incision is made in the foetal scalp with a lancet and about 100µl of blood is taken and analyzed by a micro blood sampler. It assesses foetal wellbeing by determining the current acid-base regulation. Usually pH and Base excess - levels are taken into account when deciding upon subsequent delivery procedures. The lactate level is also routinely determined but has never been considered a decision-making factor. High lactate levels are a sign of a metabolic acidosis and have as such been recorded in cases of hypoxic infants. In addition to a few publications reporting findings of high lactate level in cord blood sampling, a retrospective study has been made to detect the value of lactate in foetal scalp blood sampling.

Objective: Aim of this study was to evaluate a lactate level that assures non-pathological foetal outcome.

Method: In a retrospective study data of 1200 labours were screened. Finally 767 complete data sets of foetal scalp blood analysis were included in the analysis. Collection was performed at the Department of Obstetrics and Gynaecology, Medical University Graz during a period from 2004 to 2007. Lactate, pH and BE levels and the foetal outcome were compared to determine the significant value of lactate which predicts foetal wellbeing during delivery. The pH and lactate concentrations in these examinations were determined only in specific cases. Outcome variables were based on Apgar 1 score =< 7.

Results: Scalp blood lactate concentration and pH were simultaneously obtained in order for these two laboratory values to be compared correctly. Significant indirect correlations were evident between pH and lactate values and also between lactate level and Apgar 1. In order to guarantee an Apgar 1 = > 7, a lactate level of no more than 4.2 mmol/l was determined.

Conclusion: The lactate level in foetal scalp blood sampling is a significant indicator for foetal wellbeing and outcome. A lactate level of 4.2 mmol/l or greater is a clear indicator that the foetal wellbeing is non-satisfactory and a possible invention might be necessary.

Inhaltsverzeichnis

Glossar und Abkürzungsverzeichnis

- AD - Anno Domine
- AFI - amiotic fluid index
- BC - before Christ
- BE - Base excess
- Cit. - Citation
- CT - computerized tomographie
- CTG – Cardiotokographie; This term will frequently used and may summarizes the terms " non stress test", "contraction stress test" and "Foetal heart rate pattern monitoring"
- D - diastolic
- DMed - Doctor of medicine
- DNA - desoxyribonucleic acid
- EEG - Electroencephalography
- FGR - foetal growth restriction
- FHR - foetal heart rate
- FSB - foetal scalp blood
- FSBA - foetal scalp blood analysis
- FSBS - foetal scalp blood sampling
- GA - gestation age
- HB - Hepatitis B
- HIV - Human immunodeficiency virus
- IVF - in vitro fertilisation
- MCP - mother child pass
- Pa - per anno
- Pg - page
- S - systolic
- S:D ratio - systolic:diastolic ratio
- SFH - Symphysis fundal high
- SGA - small for gestation age
- UK - United Kingdom
- USA - United states of America

Abbildungsverzeichnis

Tabellenverzeichnis

1. Introduction

1.1 History - Background

Traditionally, obstetrics is defined as the surgical specialty dealing with the care of a woman and her offspring during pregnancy, childbirth and the puerperium, although in ancient times surgical intervention did not exist. Hippocratic physicians entered Rome in the first century BC. Their new medical knowledge was welcomed and adapted to local culture.

Midwifery and obstetrics are distinctly different but do overlap medical knowledge that focuses on the care of pregnancy and labour. Obstetricians apply the principles of rational medicine to pregnancy and confinement. Midwifery emphasizes the normality of pregnancy along with the reproductive process.

Originally, it was men who were responsible for the labour and delivery process, but because women were more knowledgeable of the experience of labour, they began studying midwifery in order to support women physically and socially. Hospitals did not exist so delivery took place in the home of the expectant mother with a midwife and the presence of other females to aid her.

Soranus (ca. 100 AD) had already described *three main stages of pregnancy*:

The first two: Conception, which required keeping the male seed within the womb and pica which occurred 40 days into pregnancy and included symptoms of nausea and cravings for extraordinary foods. During this phase women were also instructed to exercise and sleep more in order to build up strength as preparation for the labour process. The last stage of pregnancy was described as the process of delivery. In preparation for labour, the woman was advised to bath in wine and sweet-water baths in order to calm her mind before delivery. Her belly was then rubbed with oils to decrease the appearance of stretch marks and her genitals were anointed with herbs and injected with softeners such as goose fat.

1.1.1 Death and Childbirth

Mortality is considered to have been quite high in antiquity. In the ancient literature different cases are described such as Caesar's daughter Julia, who died in childbirth. Pliny, the Younger reports that both daughters of his friend Helvidius also died while giving birth.

This is caused by a few factors: a lack of sanitation and hygienic awareness, no understanding of micro-organisms and a lack of effective drugs all contributed. In the context of childbirth, however, maternal and infant mortality were seriously reduced by modern standards. [1]

To demonstrate the situation in Europe in former times, data from Britain are presented:

From 1847 to 1936 the maternal mortality rate remained virtually unchanged at around 1 death in 250 births / pa. After 1936 it fell in a very impressive way. This sharp abatement is mostly dismissed as part of a general improvement in public health, but there are other contradictory factors, such as infant mortality, which also steadily decreased during the 20th century.

Before 1936

During these times nearly all deliveries used to take place at home. The maternal mortality rate was high and this was probably caused by the general practitioner obstetricians, who used forceps under chloroform anaesthesia in up to 70% of labours. But the continual development in education saw midwives being trained in 1920 and in 1929 the British College of Obstetricians and Gynaecologists was founded.

After 1936

In 1936 there was a great breakthrough by the introduction of sulphonamides. This antibiotic was followed by penicillin and other powerful medicine. As sepsis was by far the largest factor in maternal mortality, the frequency of these deaths fell quickly.

Listed below are some important factors:

- Safer blood transfusion
- Ergometrine, for the treatment and prevention of postpartum haemorrhage
- Better treatment of pre-eclampsia and prevention of eclampsia
- Better contraception leading to reduced family size
- *Confidential enquiries into maternal deaths* – a national system, which was set up in England and Wales in 1951. Therefore enquiries are conducted by clinicians. Full investigation into every death during pregnancy or within a year after delivery. A form is filled in by all staff involved and sent to regional assessors in obstetrics, pathology and other specialties if appropriate. The data are then sent to the Department of Health for further analysis by national assessors. [2]

Maternal

Traditionally Maternal death is clearly defined. This is important to enable comparison of data over time and between countries.

Definition of maternal death

"Death of a woman while pregnant or within 42 days of termination of pregnancy from any cause related to, or aggravated by, the pregnancy or its management, but not from accidental or incidental causes"

This was recently sited by James Drife in his textbook "Clinical obstetrics and gynaecology ed." in 2007, pg 303, 6.[3]

In England during the eighteenth-century, maternal mortality was averaged at 25 per 1000 births [1]. Since 1985, the overall rate has remained constant at around 10/100 000 maternities.

Risk factors:

Age and parity - In 1999 the maternal mortality rate among women over 40 years old was 35.5% while among women aged 20-24 it was 7.2% word wide.

Social class - In 1997-1999, a similarity of the maternal mortality rate in the lowest social class in Britain, which includes itinerant and unemployed people, to that of the Third-World countries, was revealed.

Ethnicity – In the UK, the maternal mortality rate was reported to be two or three times higher among black and Asian women than among whites. Also, other countries (including USA, France and The Netherlands) have reported higher maternal mortality rates among black women.

Causes of death

The most common causes of indirect death in Britain are:

- Cardiac disease
- Psychiatric

The most common causes of direct death in Britain are:

- Bleeding - post partum haemorrhage
- Thromboembolism
- Hypertensive disease
- Ectopic pregnancy

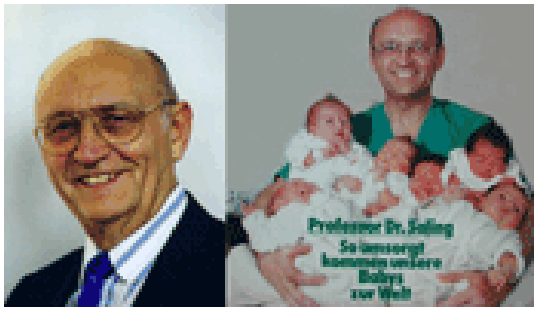
Infant

The representation of infant mortality in ancient times is complicated by infanticide and detection of it [4]. Cornelia (ca. 300 BC) the mother of Tiberius Gracchus gave birth to 12 children but only three survived into adulthood.[1]

While it is difficult to construct actual figures of the infant mortality rate in antiquity, comparisons have been made between ancient societies and modern non-industrialized societies. The figures suggested for these are then compared with those of modern industrialized societies to put them in perspective. While infant mortality is less than 10 per 1000 in modern industrialized societies, non-industrialized societies display rates from 50 to 200+ per 1000. Scholarship using model life tables and assuming life expectancy at birth of 25 years produces the figure of 300 per 1000 for Roman society [1].

1.1.2 Prof. Dr. E. Saling – "Father of perinatal Medicine"

Fig 1) Prof.Erich Saling [5]



Curriculum vitae

Erich Saling, Professor Doctor, Obstetrician and Perinatologist, was born in Stanislau (now the Ukraine) on 21st July 1925. He is the son of Heinrich Saling, a forester and his wife, Emma. In 1952 he married DMed. Hella Weymann. They have two sons, Peter, born in 1954 and Michael, born in 1955.

Erich Saling studied medicine at the University of Jena and at the Free University of Berlin from 1946 to 1952. He trained in obstetrics and gynaecology at the Women's Hospital in Berlin from 1954 to 1958. He admitted as a University Lecturer in 1963 and a Professorship at the Free University of Berlin in 1968 followed. Erich Saling became the Director of the Institute of Perinatal Medicine of the Free University Berlin and of the Department of Obstetrics in the Women's Hospital Berlin in 1976. In addition to his clinical practice he had been involved in research in the field of obstetrics and perinatal medicine since 1958. More than 550 of his publications on the subject of obstetrics and perinatal medicine have are released. The first direct examination of an unborn child was performed in 1960 by Prof. Erich Saling. The "*foetal micro blood analysis*" opened the door to the *"perinatal medicine"*.

The foetal blood sample (FBS) was introduced into clinical practice for pH measurements in 1962 as the first invasive foetal monitoring tool. [6] This methodology was an important step forward to understanding the effect of labour on blood gas homeostasis of the human foetus, and for defining the importance of foetal heart rate (FHR) patterns [1,2] revealed by continuous FHR measurement techniques, which were introduced at about the same time. [7]

The technique of foetal blood sampling has since become the ideal method of identifying intrapartum foetal hypoxia. Arbitrarily, a pH < 7.2 was chosen as cut-off value to recommend intervention. [8, 9]
This development was followed by many studies to facilitate a more exact value to ensure foetal wellbeing.

The term *"Perinatal Medicine",* was introduced by Prof. Saling in 1967 and has become widespread all over the world. This special subject deals with mothers and infants before, during, and after birth.

He also is the founder of the first national, as well as the first international, *Society of Perinatal Medicine.* His significant donations led to the expansion of this speciality. On account of his commitment, the international community of colleagues calls him the "*Father of Perinatal Medicine".*

Honours

In 1968 Prof. Saling founded the first international society, the European Association of Perinatal Medicine, and was appointed it's President In 1973 he also published the first international Journal in this field called *"Journal of Perinatal Medicine"*. In 1990 the German Society of Prenatal and Obstetrical Medicine was founded and he is also the Founder-President of this association.

In 1988 the Berlin Senate distinguished Professor Saling by awarding him the *Ernst-Reuter Medal* for his services. In 2001 he was decorated with the First Class Cross of Merit or the *Order of Merit of the Federal Republic of Germany*, by the President of the German Republic, Johannes Rau. As a special honour the *"World Association of Perinatal Medicine"* established an award named after Prof. Saling in 2000. This award is given

every two years to the best scientist in the field of perinatal medicine. In May 2005 he was elected as president of the newly founded *"International Academy of Perinatal Medicine"*.

From the 70's until retirement Prof. Erich Saling was the Director of the Institute of Perinatal Medicine of the Free University of Berlin and the Director of the Department of Obstetrics in the Community Hospital Berlin (Germany). During his administration more than 60.000 children were born. In order to be able to continue his work to improve the health of mother and child he founded the non-profit *"Erich Saling Institute of Perinatale Medicine."* Even after "retirement" he went on to developed one of his best achievements: *"The Self-Care-Program for pregnant women"*. [5]

1.2 Today

1.2.1 The mechanism of labour

"The difficulty with human delivery is related to the balance between our need to run - and therefore have a narrow pelvis - and our need to think - and therefore have a big head."

This was recently sited by James Drife in his textbook "Clinical obstetrics and gynaecology ed." in 2007, pg 393, 5. [3]

Normally apes are able to give birth without any difficulties. The foetal head is relatively small, the pelvises of the animals are relatively large, and the foetus is born facing towards the front. During the evolution of Homo erectus and the Homo sapiens in the last 1.5 million years, the brain volume has increased from approximately 500 ml to 1000-2000 ml, thus making the head bigger than the pelvis. (*"cephalopelvic disproportion").* In contrast to the apes', human labour is more difficult.

It is impossible to define a "normal" length of time for labour. The mean duration of primigravid, and second labours is between five and a half and 10 hours, but even after 40 hours of labour, a vaginal delivery is still possible (50% probability). [3]

Summarized normal human childbirth is categorized in three stages of unequal length:

- First stage: *From the onset of labour to effacement and then dilatation of the cervix*
- Second stage: *From complete cervical dilatation until the head has been delivered*
- Third stage: *From delivery until birth of the placenta and membranes* [12]

First stage: From the onset of labour to effacement and then dilatation of the cervix

The cervix is made up of a network of collagen fibres inbuilt in proteoglycans and this network needs to soften and efface by the increasing prostaglandins before labour can commence. The result is an overall reduction in the firm collagen fibres that leaves the cervix softer and ready to dilate.

2 Phases: (a) Latent: beginning of contractions until effacement of the cervix

(b) Active: the fully dilatation of cervical

Second stage: from complete cervical dilatation until the head has delivered

This process needs efficient uterine activity and is supported by "moulding" the foetal head. As the individual skull bones are unfused, their moulding and moving, or even overriding each other is possible. Moulding facilitates a successful delivery.

The infant needs to pass through the pelvis.

2 Phases:

(a) Propulsive: beginning with the total dilatation until the head has descended to the pelvic floor

(b) Expulsive: from the beginning of the irresistible desire of the mother to bear down and push until she gives birth to the baby

Third stage: From delivery until birth of the placenta and membranes

The contractions of the uterus shear the placenta from the uterine wall. This process is often indicated by a small rush of dark blood and a "lengthening" of the cord. To encourage the process, the placenta can be delivered by careful cord tractions, but it is necessary to take care not to induce uterine inversion. [3]

Problems may appear if these criteria are not fulfilled.

Possible Consequences: *Chapter 1.2.2.2 –,pg. 33.*

In some cases, childbirth is achieved through caesarean section, the removal of the neonate through a surgical incision in the abdomen, rather than through vaginal birth.

1.2.2 Imaging, monitoring and care

Normally pregnancies are uneventful and uncomplicated and usually would progress without medical intervention. In today's society, medical science has developed a number of procedures to monitor pregnancy, childbirth and the puerperium. The use of advanced medical technology is a basic component of maternal and infant health care.

1.2.2.1 Antenatal care

The western care is provided by a combination of midwives, obstetricians, family doctors and hospital visits, depending on those who need more intensive input. One main purpose of antenatal care is to identify the small number of pregnancies which develop complications, to ensure the optimal outcome for mother and baby. Care is usually based on a long established arrangement of antenatal visits.

A minimum of 5 visits during pregnancy are recommended.

The schedule varies with the initial visit usually between 10^{th} and 16^{th} weeks with subsequent visits monthly until 30 weeks, then fortnightly until 32^{nd} week and then weekly thereafter.

The initial visit before the 16^{th} week of pregnancy ("MCP-Examination")

The pregnant woman is asked to keep the antenatal record, which constitutes a medical history and physical examination, upon her initial visit to her obstetrician or midwife. The woman also receives a mother-child pass (MCP), which was introduced in Austria in 1975. Every visit during pregnancy is documented in the MCP including delivery, as well as the subsequent examinations of the child until he or she is 62 months old. This facilitates the detection of possible risk factors.

Anamnesis

- Age of mother
- Her past obstetric history
- Medical and surgical history (hypertension, diabetes, heart disease, bronchial asthma, surgeries, alcohol or nicotine abuse, abortion, IFT and IVF histories eclampsia or existing pre-eclampsia etc.)
- Family history (hereditary health abnormalities, other diseases, etc.)
- History of present pregnancy (date of the first day of the last menstrual period, regularity, due date, etc.)
- Drug history

General Examination

- Pulse rate recorded
- Blood pressure should also be monitored, and may be up to 140/90 in normal pregnancies. (High blood pressure indicates hypertension and possibly pre-eclampsia, if severe swelling (oedema) and spilled protein in the urine are also present.)
- Baseline weight
- Physical examination: Auscultation of the heart may detect structural problems, abdominal examination to measure uterine size
- Urine analysis - The purpose of this examination is to check the urine for protein and glucose.
- Vaginal examination (cytology and colposcopy upon initial visit)
- Symphysis-Fundal height (SFH; in cm) should be rechecked and compared against the relevant gestational age chart. The foetal growth is then plotted on a curve during subsequent antenatal visits.
- Measuring pelvic

- Booking blood samples

1. Exclusion of maternal anaemia and thrombocytopenia
2. Blood group to determine the ABO and Rhesus factor of the mother and to detect the presence of any irregular antibodies.
3. Serology of Rubella, Hepatitis, Syphilis, Lues and HIV

- Leopold manoeuvre

The foetus is palpated by the midwife or obstetrician using *Leopold manoeuvre* to determine the position of the baby. The Leopold manoeuvres are named after the gynaecologist, Christian Gerhard Leopold. The manoeuvres consist of 5 actions which help the midwife and the obstetrician determine the position and presentation of the foetus in the mother's uterus. It also helps to determine whether complications might develop during delivery, and if a caesarean section might be necessary.

On all subsequent visits, the gestational age (GA) is monitored.

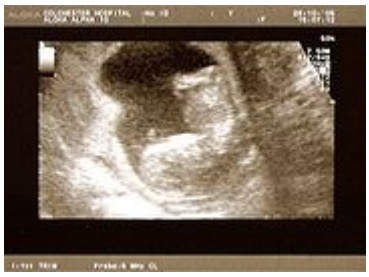
Imaging

Ultrasound scans:

Imaging is another important way to monitor pregnancy. Usually mother and foetus are also imaged in the first trimester of pregnancy. This is done to predict possible health problems of the mother. This investigation establishes foetal viability. It confirms that the pregnancy is inside the uterus (as opposed to ectopic pregnancy) and allows estimation of the gestational age (crown-rump length) after week 6. It also excludes multiple pregnancies or determines the number of foetuses and placentas. It is also possible to evaluate an ectopic pregnancy and to assess early signs of anomalies. The examination is also an opportunity for measuring nuchal translucency. Ultrasound scan can be done at any time throughout the pregnancy but it is usually conducted during MCP-examinations. [3]

X-rays and computerized tomography (CT) are not used, especially in the first trimester, because the ionizing radiation has teratogenic effects on the foetus. Instead, ultrasound is the imaging method of choice in the first trimester and throughout the pregnancy, because it emits no radiation, is portable, and allows real time imaging.

Fig 2) A dating scan at 12 weeks [10]



MCP-Examination between 16th - 20th week of pregnancy

- Foetal Ultrasound-Scan

In this examination the heartbeat is rechecked. Now it is also possible to scan the foetal abdominal circumference, head circumferences, femur length and also foetal weight is calculated to the percentile chart for the sex of the foetus. The longest column of amniotic fluid is measured for amniotic fluid index (AFI) and the placenta is localized.[3]

- General examination (as mentioned above)

MCP-Examination between 25th - 28th week of pregnancy

- General examination
- Blood samples (serology of HB-antigens = Hepatitis B-antigen, Rhesus factor antibodies, plus Rhesus-prophylaxis, if necessary)

MCP-Examination between 30th - 34th week

- General examination
- 2nd foetal ultrasound-scan
- Toxoplasmosis scan (Recheck)

MCP-Examination between 35th - 38th week of pregnancy

- General examination [2]

A more detailed examination will be made upon conspicuous diagnostic findings:

Doppler flow velocity wave forms:

Waveforms of different types are caused by the utero-placental and foeto-placental circulation. These are low resistance systems in which the flow of blood towards the placenta continues throughout the cardiac cycle. In the case of an increasing resistance due to utero-placental atherosclerosis, and/or foetal disease of unknown cause, these waveforms may change. It is important to determine the difference between the peak systolic flow (S) and the end-diastolic flow (D). In case of an increasing S:D- ratio, it is more likely that the foetus is compromised, particularly if end diastolic flow is absent or reversed or if the S:D-ratio is extreme.

This facilitates the identification of a major defect in foeto-placental perfusion, which could be associated with intrauterine growth restriction and pregnancy-induced hypertension before the 34th week of pregnancy. Summarized, this examination is a useful method to identify insufficient placental functioning, and determines the foetus wellbeing. [3]

Amniocentesis

Genetic counselling is often offered for families who may be at an increased risk of having a child with a genetic condition. Amniocentesis is sometimes done for women at around the 20th week, if they are 35 years of age or older. This examination is to check for Down's syndrome and other chromosome abnormalities in the foetus. Amniocentesis is a prenatal genetic screening of the foetus, which involves inserting a needle through the mother's abdominal wall and uterine wall, to extract foetal DNA from the amniotic fluid. There is a risk of miscarriage and foetal injury during the examination because it involves penetrating the uterus while the baby is inside.

Triple Test

Even earlier than amniocentesis, the mother may undergo the triple test. Nuchal fold, nasal bone, alpha-fetoprotein are screened. This is also to check for disorders such as Down syndrome.

Possible antenatal complications:

- Gestational hypertension and pre-eclampsia
- Foetal growth restriction (FGR) and small for gestational age (SGA)
- Impaired glucose tolerance and diabetes disease
- Haemolytic disease
- Breech presentation
- Anaemia
- Polyhydramnios
- Prolonged pregnancy (> 42 weeks)
- If there is a prolonged pregnancy, labour should be induced by local drugs placed vaginally. It has been shown that this intervention reduces foetal distress and meconium staining compared with pregnancies followed only by monitoring. The local drug interventions effect a reduction in the caesarean section rate. There is no demonstrable effect on perinatal mortality, and it has been even estimated that 500 inductions may be required to prevent one perinatal death.

1.2.2.2 Perinatal care – focus on FSBA

- **Vaginal examination**

Depending on progress this examination should be performed every 2 - 4 hours, ideally every examination should be carried out by the same person to minimize the subjective element of interpretation. It is important to examine the cervical dilatation and monitor the descent of the foetal head.

The mean cervical dilatation in primgravid mothers is approximately 1 cm per hour and the descent of the foetal head is recorded with respect to the ischial spine

- **Foetal heart rate recording**

This examination has been in use since the 1950s. It has a good sensitivity but a poor positive predictive value in determining foetal distress during labour.

Procedure:

- Intermitted monitoring
- Continuous monitoring

It is a record that is recorded by two separate transducers, which can be positioned externally on the mother's abdominal wall or internally by dilating the cervix. One transducer is an ultrasonic heart rate sensor which is for the measurement of the foetal heart rate. The latter is a pressure sensitive contraction transducer in order to record the uterine contractions.

This examination is a foetal heart monitoring which records FHR in relation to uterine contractions. The abnormal patterns are shown in **Tab. 1**.

Interpretation:

Healthy patients were defined as those in whom the baseline FHR lay between 120 and 160 beats / min, thereby including no decelerations.

For the interpretation of foetal heart rate pattern, it is important to know:

If hypoxia occurs, the beginning of tachycardia is delayed and may persist for 10-30 min thereafter. The vagal response predominates during moderate or severe hypoxia. Unlike tachycardia, bradycardia is a rapid response of a hypoxic episode and lasts as long as the hypoxic event continues. After the event it ceases. [3]

The interpretation of FHR - pattern maybe made by means of the "Fischer Score" (Wolfgang M. Fischer 1976). *See next page.*

Interpretation of results based on the 5 criteria of the Fischer Score:

Tab 1) 5 criteria of Fischer score

	Normal	Indeterminate	Abnormal
Baseline heart rate	110-150 bpm	100-109 or 151-170 bpm	<100 or >170 bpm, sinusoidal foetal heart rate
Variability	>= 5 bpm	< 5bpm for more than 40 min or > 25bpm	< 5bpm for more than 90 min
Zero-Crossing	>=6	/	< 6
Acceleration	2/ 20 min	periodical to contractions	no accelerations > 40min
Decelerations	None or DIP 0	DIP I additional to other conspicuous criteria	DIP II, decelerations > 3min

Definition:

bpm: baseline per minute

Acceleration: a rapid acceleration of the foetal heart rate for more than the normal variability

Deceleration: a rapid deceleration of the foetal heart rate for more than the normal variability

DIP- **D**ecelerations **I**n **P**ressure

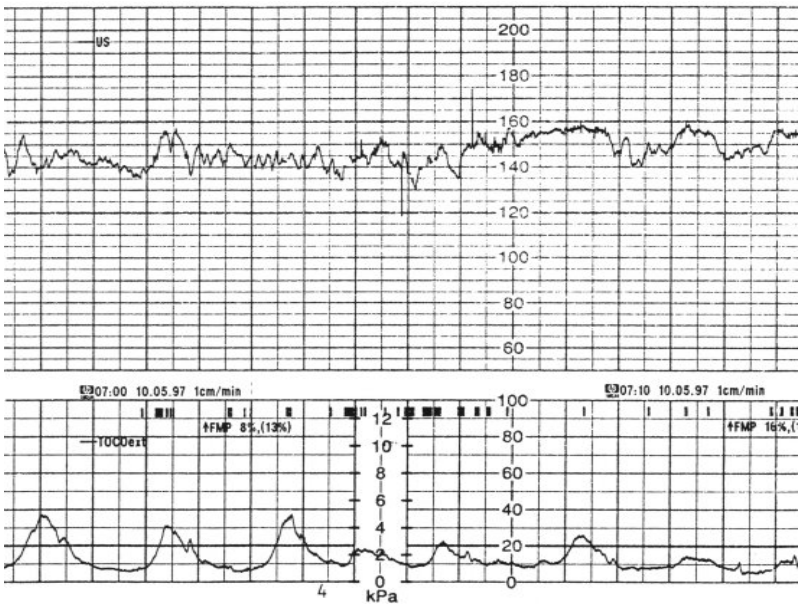
DIP 0 = chronologically independent uterine contractions; **DIP 1** = the DIP occurs in the early stages of uterine contractions. This is probably due to pressure on the foetal head during a contraction and it has no prognostic significance. **DIP 2** = this deceleration starts late during uterine contraction and persists after the contraction ended. This identifies impairment of the utero-placental blood flow, a reduced foetal oxygenation and as a consequence, foetal hypoxia.

Variability: Normally the beat-to-beat heart rate shows a variability of more than 5 bpm. This causes a wavy line on the trace. A reduction, or absence, indicates some degree of foetal hazard.

=> If the FHR - pattern is not pathological, there is a high reliability of foetal wellbeing.

=> In case of pathological changes, close monitoring is required. [3]

For Example **Fig 3**) CTG trace [11]



- **Foetal scalp blood analysis (FSBS)**

General

If hypoxia persists, acidaemia develops after a certain time. The more often acidaemia develops, the higher the risk of foetal death. FSBS determines pH, lactate, pCO^2, pO^2 and BE-levels and in particular, defines the degree of acidaemia. [11]

Indications

- persistent variable or late decelerations on CTG
- persistent foetal tachycardia
- prolonged and persistent early decelerations
- Significant meconium stained liquor (grade 2 or 3) along with any CTG abnormalities
- Prolonged loss of baseline

Contraindications

- Risk of infection transmitted from the mother (for example HIV, Hep B, Herpes or group B of Beta-haemolytic streptococci)
- Foetal bleeding diathesis (for example von Willebrand´s Disease)
- Severe premature birth (for example before 32-34 weeks) [3]

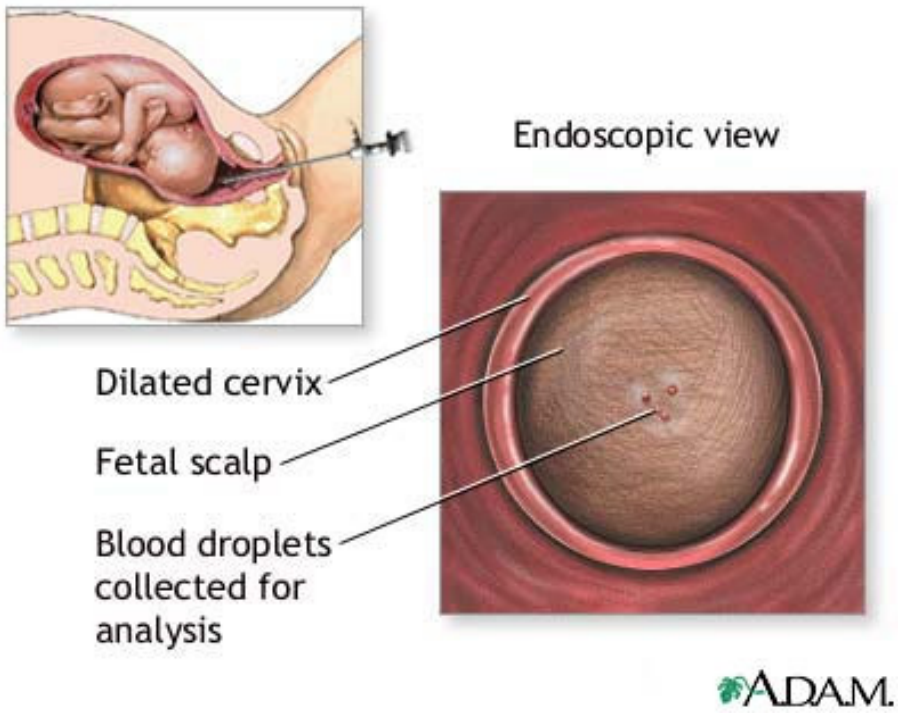
Procedure

For the examination it is necessary to place the mother in the lithotomy position with 15 degree lateral tilt. Therefore the pregnant woman is laid on the back with knees bent, positioned above the hips, and spread apart through the use of stirrups. Upon approaching full dilatation, the woman is positioned in the left lateral position.

Foetal scalp blood sampling requires the cervix to be dilated at least 4 to 5 cm and the vertex at a station 1 or below to accomplish this. If the membranes have not

already ruptured, they are deliberately punctured. A tubular speculum is inserted through the cervix. Mineral oil or similar lubricate is applied to the scalp. After this, the instrument is pressed on the foetal scalp, and a small incision is made with a lancet. Blood is then collected in a long capillary tube, which should hold about 100µl of fluid. To perform a single pH test 30µl is needed, and 70µl to determine both the pH and pCO^2. The latter is important to determine if the acidosis is metabolic or respiratory nature. This is an important question, because respiratory hypoxia is far less dangerous than a hypoxic introduced metabolic acidosis .[12]

Fig 4) Procedure of FSBA [13]



Interpretation

- *standard value*

  pH: 7.25-7.35 (mean 7.33)

  pCO^2: 40-50 mmHg

  pO^2: 20-30 mmHg

  Base Excess : -3 - +3

- *Non-reassuring findings (see interpretation below)*

  pH: 7.25 – 7.20

  Base Excess - 6 - +6

- *Metabolic Acidosis*

  pH: < 7.20

  pCO^2: 45-55 mmHg

  pO^2 < 20 mmHg

  Base Excess > - 2

- *Respiratory Acidosis*

  pH < 7.25

  pCO^2 >50 mmHg

  pO^2 varies

  Base Excess > + 2

=> *Possible influences on the result*

- An important interacting factor is *the mother's acid-base status.* The mother's condition could have deteriorated through sepsis, ketoacidosis, dehydration or hyperventilation (which decreases the baby's HCO^3 intake)
- Also *the perfusion of the issue* influences the acid-base status of the baby [14]

=> *Risks and adverse effects of FSBA*

1. The baby may be hurt and suffering pain - some times there are signs of stress, e.g. excess movement – kicking , and foetal heart rate acceleration
2. Intermittent observation
3. Foetal scalp haemorrhage - bleeding may be difficult to control
4. Analysis of pH is complicated, however, and needs a relatively large amount of blood (30-50µl), and sampling failure rates of 11-20% have been reported. [9, 10] The findings also do not always discriminate between respiratory and metabolic acidaemia, the latter being associated with neonatal morbidity. [15-17]

Summarized:

Tab 2) Clinical guidelines for foetal scalp blood sampling (FSBS) pH and lactate [18]

	pH	Lactate (mmol/L)
Normal	>7,25	< 4.2
Pre-acidaemia / Pre-lactemia	7.20-7.25	4.2-4.8
Acidemia / Lactemia	<7.20	> 4.8

Consequences:

- Scalp pH > = 7.25 and FHT remains non-reassuring

=> Continue to observe labour

- Scalp pH 7.20 – 7.25, or lactate of ~ 3.5 - 4.1 and FHR remains non- reassuring

=> Borderline

=> Repeat scalp sampling in 30-60 min, but if there are no other adverse effects to deliver the foetus quickly, the labour may continue while close surveillance is maintained

The mother should be repositioned if in the first stage of labour. Although the benefit of it is debatable, she may be given oxygen (via face mask). In case of strong uterine contractions caused by an oxytocin infusion, the drip should be slowed or stopped. After this, it is necessary to observe the labour procedure continually. It is important to pay attention to the monitor tracing whether the foetal heart pattern reverts to normal or not. If it does not and there is evidence of an increasing foetal acidosis, then the baby must be immediately delivered by operative intervention.

- Scalp pH < 7.20 or scalp lactate of > 4.2 mmol/l – is consistent with foetal acidosis

=> Immediate delivery

An instrumental vaginal delivery should be performed, if the patient is in the second stage of labour and the foetal head is in an occipital-anterior position.

The baby is best delivered by caesarean section if the head of the infant is in a posterior or transverse position [2, 3]

Definition of the different values

- pH

pH was originally described by Danish chemist Soren Peder Lauritz Sorensen at the Carlsberg Laboratory in 1909.

The pH level measures the activity of dissolved hydrogen ions (H^+). Consequently it is a measure of the acidity or alkalinity of a solution. The coefficients measurement of hydrogen ion activity is based on theoretical calculations. The pH scale is based on a set of standard solutions established by international agreement. A solution with a pH of less than 7 is called an *acidic* solution. A solution with a pH of more than 7 is called an *alkaline* solution.[19]

Physiology

The pH of different cellular compartments, body fluids, and organs is usually tightly regulated in a process called acid-base homeostasis. The pH of blood is usually slightly alkaline with a value of pH 7.37. This value is often referred to as a *physiological pH* in biology and medicine.

To keep the physiological pH balanced, there are few buffering agents (for example bicarbonates) in the human body which reversibly bind hydrogen ions and impede any change of pH. If the imbalance overcomes the buffering system, it can be compensated by changing the frequency of ventilation.

$$\mathrm{HCO_3^- + H^+ \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O}$$

In the body, pH can be estimated from prevailing base excess (BE) and bicarbonate concentration (HCO^3) by the following equation:[20]

$$pH = \frac{be - 0.93HCO_3 + 124}{13.77}$$

Acidosis: The most common disorder in acid-base homeostasis is acidosis, which means an acid overload in the body, generally defined by arterial pH falling below 7.35.

⇒ Metabolic acidosis (increasing H^+ and loss of bicarbonate)

⇒ Respiratory acidosis (decreased respiration causes increased carbon dioxide and decreased pH)

Alkalosis: Defines an excess of base and generally an arterial pH of more than 7.45.

⇒ Metabolic alkalosis (decreased hydrogen ion concentration leads to increased bicarbonate concentration)

⇒ Respiratory alkalosis (increased respiration causes elevated pH)

Possible Consequences:

⇒ Plaque can create a local acidic environment that can result in tooth decay by demineralization.

⇒ Enzymes and other proteins have an optimum pH range and can become inactivated or denatured outside this range.

⇒ General symptoms of acidosis resulting from decreased pH in body. [21]

- **BE**

The concept of "*base excess*" was first introduced by Astrup and Sigaard-Andersen in 1958.

This value refers to the amount of acid that is needed to return an individuals' blood pH from abnormal to the pH reference range (7.35 - 7.45) provided that the standard value amount of carbon dioxide is upheld.. Another possible definition of "base excess" is: the amount of acid or base that must be added to a litre of blood (ECF) to return the pH to 7.4 provided that the pCO^2 is stable at 40 mmHg (5.3 kPa).

Calculation

The concentration of current base excess in blood (ABEc) and HCO^3 - are derived parameters, calculated from pH and $PaCO^2$ values and a photometric haemoglobin measurement.

c denotes concentration, and *ct*Hb the total concentration of haemoglobin (deoxy-, oxy-, carboxy-, met- and sulph- haemoglobin)

$$Base\ excess = 0.93\ (HCO_3 - 24.4 + 14.8\ (pH - 7.4)) \quad [22]$$

Interpretation:

Current base excess is simply the prevailing base excess in the blood.

Standard base excess is the value of base excess when the haemoglobin value is 5 g/dl. This gives a better insight to the base excess of the entire extra cellular fluid.

It is common practise to report BE in units of *mEq/L.* The physiological reference range is between -3 and +3.

For example:

In the case of BE = 2: this stands for a physiological condition that has 2 parts more base than acid, which defines an alkalotic acid/base disturbance.

A possible cause for BE < -3

- Lactate acidosis (for example after anaerobic metabolism during heavy exercises)
- Diabetic ketoacidosis

A possible cause for BE > 3

- Persisting vomiting causing loss of acidic gastric fluids

- **Definition of partial pressure**

Partial pressure is defined as the pressure of a certain amount of gas which occupies a particular volume while retaining a constant temperature. Subsequently, the sum of all partial pressures of in a gas mixture is defined as the *total pressure.* The partial pressure is a measure of thermodynamic activity of the gas's molecules.
The value varies geographically and with time, and also varies in different organism tissues. [21]

⇒ **PCO^2**

- Partial pressure of carbon dioxide

Carbon dioxide is a chemical bond composed of two oxygen atoms compounded with a single carbon atom. It is soluble in water, in which it spontaneously alternates between CO^2 and H^2CO^2 (carbonic acid). The concentration of these two compounds and the de-protonated forms of HCO^{3-} (bicarbonate) and carbonate depend on the current pH.

Physiology

The human's breathing rate influences the concentration of CO^2 in the blood. More precisely, breathing is stimulated by a higher carbon dioxide level. Normally the gas we exhale has a concentration of carbon dioxide of about 4-5%.

In blood, CO^2 is transported in 3 different forms:

- 70-80% is converted by the enzyme carbonic anhydrase to HCO^3- (bicarbonate ions) in the red blood cells. The reaction: $CO^2 + H^2O \rightarrow H^2CO^3 \rightarrow H^+ + HCO^{3-}$
- 5-10% is dissolved in the plasma
- 5-10% is linked to haemoglobin and carbamino compounds

Important effects:

- Carbon dioxide inhibits the pH level from rising.
- An increased partial pressure of CO^2 or a decreased pH causes an offloading of oxygen from haemoglobin, which is known as the "*Bohr Effect"*.
- Carbon dioxide is one of the agents of local auto-regulation of blood supply –> A high concentration of it affects the expanding capillaries to facilitate higher blood flow to the tissues. [23]

⇒ **PO^2**

- Partial pressure of oxygen.

Oxygen is a colourless, odourless, tasteless, non-metallic, gaseous element. It is the most abundant element in the earth's crust (almost 50% of it's mass), forms about 21% volume of the atmosphere, and exists in bounded form in water and many other substances. Oxygen is a by-product of photosynthesis and the basis for respiration in plants and animals. In nature it exists as a molecule composed of two atoms => O^2.

Physiology

Normally the gas we inhale has a concentration of oxygen of about 20,9%. The human's breathing rate influences the concentration of O^2 in the blood.
Oxygen is compound reversibly to erythrocytes (in particular to haemoglobin) in human blood to be transported to the peripheral tissues.

Interactive characteristics:

- Affinity of O^2-binding of haemoglobin decreases:

⇒ H^+ - concentration increases

⇒ CO^2 - concentration increases

⇒ Temperature increases

⇒ 2,3 - Biphosphoglycerat increases

- No oxygen-binding possible

⇒ Presence of carbon monoxide (stronger bond force)

⇒ Presence of methaemoglobin (change in structure of haemoglobin) [21]

Physiologic rationale of foetal blood sampling

During active labour the uterus contractions cause due to intrauterine pressure to exceed 30 mmHg. This provokes the arteries which are supplying the intervillous space of the placenta, to become constricted, which further results in a temporary decreased flow and a reduced exchange of oxygen and carbon dioxide to and from the foetus. This lack of oxygen can be compensation in a healthy foetal-placental unit. But this compensation only lasts 60 seconds or less, providing there is a sufficient respite for 2 minutes between the contractions. If these arterial constrictions continue, there will be an accumulation of CO^2 (hypercapnia) and a shortage of oxygen (hypoxemia). The former state causes a respiratory acidosis, whereas the latter may produce a metabolic academia.

Any incident that affects the placental blood flow and gaseous exchange during labour also affects the foetal blood gas homeostasis. Acute incidents such as an abruption, a prolapsed or compressed umbilical cord, entanglement and supine hypotension affect blood gas homeostasis more subtly, sometimes producing a respiratory acidosis before a metabolic one. Any decrease in FHR results in a) a decreased cardiac output, b) decreased CO^2 transfer, and c) CO^2 accumulation. How long it takes to develop a metabolic acidosis depends on the particular incident and the individual foetal energy reserve and its ability to compensate.

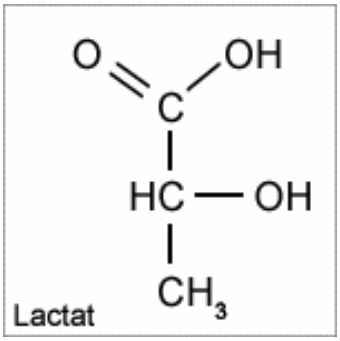
=> Energy balance and accommodation

The foetus normally derives its metabolic needs through the oxidation of glucose (or glycogen) to water and carbon dioxide in the presence of oxygen, which results in the

generation of 38 units of ATP in aerobic metabolism. A healthy foetus is able to adjust to short episodes of hypoxemia to maintain aerobic metabolism by a synchronized response that involves behavioural cardiovascular, metabolic and hormonal adjustments. [24] The most important cardiovascular response is the centralization of blood flow to the heart, brain and adrenals, with increased oxygen extraction from the placental bed and tissues. If these adjustments fail to maintain adequate oxygen supply to the central organs, aerobic metabolism is supplemented by anaerobic metabolism of glucose and glycogen. Consequently, lactic acid maintain cell and organ functions through the generation of 3 units of ATP in the Krebs cycle. Although anaerobic metabolism is much less efficient than aerobic metabolism it is nonetheless a very important survival mechanism, particularly for maintaining cardiac and brain function during hypoxemia / asphyxia. Anaerobic metabolism is largely dependent on the pre-asphyxia glycogen content of the myocardium and liver [24,25] and the long-term stores of glucose, which are depleted during this process. [26]

⇒ *How is lactate produced?*

Fig 5) Formula of lactate



Lactic acid is the main specific end-product of anaerobic metabolism and also the main biochemical marker of metabolic acidosis.

The detailed chemical process for the production is:

During the second step of the anaerobic glycolysis, 2 molecules of ATP are produced. A reduction of 2 molecules from NADH results in NAD+ which creates 2 three-carbon molecules of pyruvate. In the last step of the anaerobic glycolysis, the pyruvate is converted to lactate (the conjugate base of lactic acid) in a process called *lactic acid fermentation:*

$$\text{Pyruvate} + \text{NADH} + \text{H}^+ \rightarrow \text{lactate} + \text{NAD}^+$$

Consequently, the accumulation of pyruvic acid and lactic acid causes an increase in hydrogen ions [H+], during anaerobic metabolism, resulting in a metabolic acidosis. Free intracellular hydrogen ions are toxic to cells and are buffered by bicarbonate, haemoglobin, and plasma protein. When these buffers are saturated, there is a marked increase in free [H^+] ions and a fall in pH, followed by acidosis. This saturation occurs after hypoxemia [26]

This process of anaerobic glycolysis (either full or partial) also occurs in animals under hypoxic conditions. It is found, for example, in overworked muscles that are starved of oxygen, or in heart muscle cells after heart attack. In many tissues, this is a cellular last resort for generating energy.

For example during power exercises such as sprinting, when the rate of demand for energy is high, lactate is produced faster than the ability of the tissues to remove it and lactate concentration begins to rise. This is a beneficial process since the regeneration of NAD^- ensures that energy production is maintained and exercise can continue. The increased lactate produce can be removed in a number of ways including:

- oxidation to pyruvate by well-oxygenated muscle cells which are then directly used to fuel the citric acid cycle
- conversion to glucose via the Cori cycle in the liver through the process of gluconeogenesis [20]

Tab 3) *Current statistical facts* [27]

The FSBA in Univ. Hospital Graz (2003 - 11.9.2009)

			based on:
Labours	**13855**	**100%**	
Births	**14299**	**100%**	
CTG on admission	**13794**	**99.6%**	*pregnant women*
CTG during labour	**14120**	**98.7%**	*children*
thereof: continuous	**1514**	**10.7%**	*performed CTGs during labour*
intermitted	**8**	**0.1%**	*performed CTGs during labour*
FSBA performed	**1661**	**11.6%**	*children*
thereof:			
min pH<7	**1**	**0.1%**	*performed FSBA*
min pH between 7.00- 7.09	**11**	**0.7%**	*performed FSBA*
min pH between 7.10-7.19	**70**	**4.2%**	*performed FSBA*
min pH between 7.20-7.29	**381**	**22.9%**	*performed FSBA*
min pH=> 7.30	**1112**	**66.9%**	*performed FSBA*

Efficiency:

1. Reduces the number of unnecessary caesarean sections
2. False positive rate if scalp pH < 7.20: < 20%

- **Direct foetal pulse oximetry**

It is possible to check the foetal oxygen levels directly by placing a pulse oximeter against the foetal cheek during labour. This may be achieved by rupturing the membranes at a cervical dilation of at least 3cm. A large multicentre trial revealed reduced numbers of caesarean sections performed for uncomplicated births, examination method. But on the

other hand, the pulse oximetry also caused an increased number of caesarean sections by disturbing the birth procedure and provoking dystocia. Summarized, the effectiveness of the examination is still debateable.

Possible perinatal complications, and in particular, Asphyxia

- *Premature rupture of the membranes*

Approximately 6-12% of all pregnancies, the membranes rupture earlier than the onset of uterine contractions or cervical dilatation and is often described as a feeling of leaking fluids vaginally. During the speculum examinations, a pool of liquor in the posterior fornix may be seen.
In this particular case, one should retrain from vaginal examination, because of the increasing risk of introducing an ascending infection. In 70% of all pregnant women where this happens labour can be induced during the following 24 hours, if optimally managed. In a small number of cases, chorionamnionitis may rapidly turn into a, immense foetal and maternal septicaemia. If there are any suspicious signs of infection, e.g. pain or discharge, delivery must be induced, frequently by caesarean section. [3]

- *Hidden acidosis as a forerunner of asphyxia*

Foetal hypoxemia is caused by adverse uterine labour contractions and results in intermittent obstruction of the uteroplacental circulation and an interrupted supply of oxygenated maternal blood to the placenta. Hypoxic stress leads to an acute redistribution of foetal blood flow away from the periphery and the viscera to the vital organs, and the brain. After delivery, a kind of "tissue trapping"`- phenomenon becomes manifest when the vascular bed widens again in hypoperfused, non-priority organs and accumulated anaerobic metabolites flood into the central circulation. This process is also known as *"hidden acidosis"*. [28]

- ***Asphyxia***

Definitions

The criteria for the diagnosis of asphyxia is defined by WHO as

"Failure to initiate or sustain respiration after birth"

The *National Neonatal Perinatal Database (NNPD) 2000* uses a similar definition:

Moderate asphyxia is defined as

"Apgar - score of 4-6 or slow gasping breathing at 1 min after delivery"

Severe asphyxia is defined as an

"Apgar - score of 0-3 or no breathing at 1 min after delivery"

According to the *American Academy of Paediatrics (AAP)* and the *American College of Obstetrics and Gynaecology (ACOG)* every criterion of the following must be present for the diagnosis of asphyxia:

(1) profound metabolic or mixed academia (pH< 7.00) in cord blood

(2) persistence of Apgar - score 0-3 for more than 5 minutes

(3) neonatal neurologic sequelae (seizures, coma of hypotension)

(4) multiple organ involvement (of the kidney, lungs, liver, heart, intestine)

Possible consequences of perinatal asphyxia could be hypoxic injury to various organs including kidneys, lungs and liver, but the main hypoxic effects are visible on the central nervous system. [3]

Therapy

- acute tocolysis with atosiban or hexoprenalin and application of oxygen

A prospective randomized trial of atosiban versus hexoprenaline for acute tocolysis and intrauterine resuscitation was conducted *by Afschar P, Schöll W, Bader A, Bauer M and Winter R* in Graz, Austria. It concluded that atosiban and hexoprenaline were similarly effective for stopping uterine contractions. Different effects were apparent among women receiving atosiban, which had significantly fewer adverse effects than hexoprenaline. Uterine contractions resumed more promptly in the atosiban group. Considering the low occurrence of mild maternal adverse side-effects, atosiban might be an option for treatment of acute intrapartum tocolysis for foetal distress. [29]

- Immediate delivery

An instrumental vaginal delivery should be performed, if the patient is in the second stage of labour, the foetal head is in an occipito-anterior position and a foetal station of at least 0. The baby is best delivered by caesareans section if the head of the infant is in a posterior or transverse position and a foetal station < 0. [3]

Management of neonates with perinatal asphyxia [30]

Initial management

⇒ transfer the baby to special care newborn unit
⇒ maintain body temperature
⇒ check vital signs
⇒ start administering intravenous fluids (in severely affected babies)
⇒ Check blood sugar, hematocrit and blood gases
⇒ Miscellaneous (Vitamin K, gastric lavage in the case of meconium staining)

Subsequent management

⇒ Continue monitoring
⇒ detailed examination (EEG)
⇒ Amplitude-integrated electroencephalography (aEEG)
⇒ Cranial ultrasound
⇒ Computer tomography (CT)
⇒ Magnetic resonance imaging
⇒ Sonography

Possible organ dysfunction after Perinatal Asphyxia

CNS	Hypoxic ischemic encephalopathy, intracranial haemorrhage seizures, long-term neurological sequelae
Cardiac	Myocardial dysfunction, valvular dysfunction, rhythm abnormalities, congestive cardiac failure
Renal	Hematuria, acute tubular necrosis, renal vein thrombosis
Metabolic	Acidosis, hypoglycemia, hypocalcemia, hyponatremia
Pulmonary	Delayed adaptation, respiratory failure, aspiration of meconium depletion of surfactant, primary pulmonary hypertension
GI tract	Necrotizing enterocolitis, hepatic dysfunction
Haematological	Thrombocytopenia, coagulation abnormalities [3]

- *Prophylaxis of Asphyxia*

Foetus with high-risk of developing intrapartum hypoxia and acidaemia:

Maternal factors

=> Hypertensive disorders in pregnancy / preeclampsia
=> Diabetes
=> Multiple pregnancies

=> Severe anaemia

=> Severe malnutrition

Placental factors

=> Abruption of the placenta

Foetal factors

=> Growth restriction

=> Malpresentations

=> Cord complications

=> Clinical "*foetal disstress"* *

* Definition of clinical foetal stress is: foetal heart rate > 160 but < 110 bpm (beats per minute) persisting for 5 minutes, or meconium stained liquor. [3]

There is a test for identifying high-risk pregnancies:

- <u>*Test for foetal wellbeing in high-risk pregnancies:*</u>

In the case of a high-risk pregnancy, the test should commence after the 30th week to determine the foetal wellbeing.

⇒ Foetal movement (foetal kick) counts

In a 3-hour period, the mother counts the number of times the foetus kicks. Usually there are a number of 10 kicks, but as foetuses do not always have the same patterns of activity, the mother should also check the number of kicks during a second 3-hour period. The test should be done three or more times a week and if the foetus fails to kick at least 10 times during the 3-hour period, the doctor or hospital should be contacted.

⇒ Foetal heart rate pattern - Summary at pg. 16

⇒ Serial ultrasound examinations - Summary pg. 11

⇒ Doppler flow velocity wave forms - Summary pg. 13

The tests have a good sensitivity but a poor positive predictive value. [3]

1.2.2.3 Postnatal records

Arterial and venous cord blood sampling

With the examination of umbilical cord blood sampling after delivery it is possible to provide important data of the newborn's metabolism. The acid-base status reflects the newborn's aerobic and anaerobic intrauterine metabolisms. It is a retrospective measure of the foetal exposure and response to hypoxia. A marker of perinatal hypoxemia is a clearly elevated arterial cord blood lactate level.

Various studies had shown that the cord blood lactate level is as relevant as the acid-base balance to predict neonatal morbidity. [31]

In 2008 *N Wiberg et all.* found out about the effects of delayed umbilical cord clamping at birth on arterial and venous blood gases and lactate concentrations. It results in significantly different values of cord blood acid-base parameters. [28]

Apgar - score

This Score was established by Dr. Virginia Apgar as a simple and repeatable method to assess the health of newborn children quickly immediately after delivery. The method was devised in order to ascertain the effect of obstetric anaesthesia on newborn.

Tab 4) *The five criteria of Apgar - score:*

	Score 0	Score 1	Score 2	Component of acronym
Skin Color/Complexion	blue all over	blue at extremities, body pink (acrocyanosis)	no cyanosis, body and extremities pink	**A**ppearance
Pulse rate	absent	< 100	> 100	**P**ulse
Reflex irritability	no response to stimulation	grimace/feeble cry when stimulated	sneeze/cough/pulls away when stimulated	**G**rimace
Muscle tone	none	some flexion	active movement	**A**ctivity
Breathing	absent	weak or irregular	strong	**R**espiration

Clinical consequences:

Optimally: 9 – 10 points

Possibly dangerous: 5 – 8 points

Life-threatening: < 5 points

1.3 Aim of the retrospective study

This study was conducted to establish a context for the lactate level in labour, and the final outcome of the newborn. In order to define a cut – off level for foetal distress, one should be able to determine a lactate level during labour which ensures a satisfactory outcome for the infant.

Introduction:

Asphyxia during labour is a predominant cause of neonatal mortality, morbidity and permanent neurological disability. An early prediction of asphyxia and an intervention recommendation may prevent a possibly worse foetal outcome. The pH level as an indicator of foetal acidosis is well known, however the pH is not always clearly decreased. An additional marker would be helpful to identify the necessity of an intervention.

It is known that lactate is always produced when hypoxia or poor tissue perfusion due to anaerobic glycolysis develops If oxygen is critically reduced the Kreb's Cycle cannot sustain aerobic metabolism. This, in turn, leads to anaerobic metabolism and further to an increase in the production and accumulation of blood lactate. The anaerobic metabolism is needed by tissues to meet the energy requirements. The lactate concentration in blood can also be taken into account when evaluating critically ill and injured patients to: a) detect tissue hypoxia at an early stage, b) assess illness severity and c) predict outcome. [32]

Due to the reactions described above, lactate concentration may be a reliable indictor for asphyxia and may also be determined by the foetal scalp blood analysis. This is an invasive procedure, which is required to determine the current acid-base status.

Usually lactate, pH and base-excess levels can be determined easily. Comparisons between lactate and pH levels in scalp blood already revealed a significant correlation and subsequently a consistency in the foetal outcome.

The lactate level in the foetal scalp blood analysis as a marker of perinatal asphyxia has already been established. Multiple studies have revealed the prognostic value of lactic acidemia in newborns with serious hypoxemia. [32,33] Until now a clear lactate level which would assure a good foetal outcome was not defined.

2. Material and methods

The collection was performed at the Department of Obstetrics and Gynaecology, Medical University Graz from 2004 to 2007. In a retrospective study data of 1200 labours were screened. Finally 767 complete data sets of foetal scalp blood analysis were included in the study. Lactate, pH and BE levels and the foetal outcome were compared to determine the significant value of lactate which predicts foetal wellbeing during delivery. The pH and lactate concentrations in these examinations were determined only in specific cases. Foetal scalp blood was sampled for lactate (n = 315), pH (n = 315) and base excess (n = 314). This study was approved by the General Hospital's Ethics Committee in April 2009.

Routine procedure:

The decision to analyse the foetal scalp blood was based on the obstetrician's finding of an abnormal foetal heart rate on the CTG trace. After the women were consented to the examination, the foetal wellbeing evaluation was performed.

Description of procedure:

The midwife positions the women in the left lateral of the lithotomy position. An amnioscope is inserted into the vagina, then a small incision is made to the foetal scalp and 50µL of foetal scalp blood is collected in a glass capillary tube. Lactate levels are determined immediately after sampling.

The blood is analyzed by a ADL 800 flex Radiomet; Copenhagen, Denmark;

Then the obstetrician decides the next course of action. (Criteria are discussed at pg. 21 - *Consequences*)
After delivery, the paediatrician or the obstetrician determines Apgar - score and both umbilical arterial and venous blood gases are routinely analyzed.

The main outcome variables, which are taken into account, are: *arterial and venous pH* of *the umbilical cord*, *BE*, *Apgar - score* and if necessary, the *admission into neonate intensive care unit (NICU).*

2.1. Population of the study

Tab 5) Study characteristics

Numbers of birth, n		415	
	female	190	45,80%
	male	225	54,20%
Mean maternal age, years		28,3	from 16 to 45
			standard deviation
mean birth weight		3348,5	
	male	3411,1	482,5
	female	3271,9	478,6
Spontaneous labour, n		294	71%
Mode of delivery, n			
	breech delivery	4	1%
	operatives (forceps or vacuum)	17	4%
	Caesarean section	100	24%
APGAR =< 7, n			
	At 1 min	63	15%
	At 5 min	10	3%
	at 10 min	3	1%

2.2. Statistical analyses

The data were analysed and two graph receiver operating curves were created by using SPSS Vers. 15.0.1 and TG-ROC, software designed by M. Greiner [34]

3. Results

During a 6-months-period (April 2009-October 2009), 1200 protocols of deliveries at the Department of Gynaecology and obstetrics in Graz, Austria, were evaluated Protocols confirmed that FSBA was analysed when electronic monitoring revealed a non reassuring pattern.

The main factors which determine a satisfactory foetal wellbeing

The scalp lactate value range from 0.8 to 11.3 mmol/l
The pH value range from 6.968 to 7.508
The BE value range from 4.0 to –16.3

The main variables of foetal outcome

To differentiate several variables to classify foetal outcome:

- Apgar - score at 1 min, 5 min and 10 min
- Umbilical artery and venous pH

63 babies had an Apgar - score at 1 min < 7 (15%)

Overview of the following results of the charts:

- In the first three charts fig.***A1, A2 and A3*** the relationship between the different values, which are determined by FSBA are shown:

  $\Rightarrow pH$

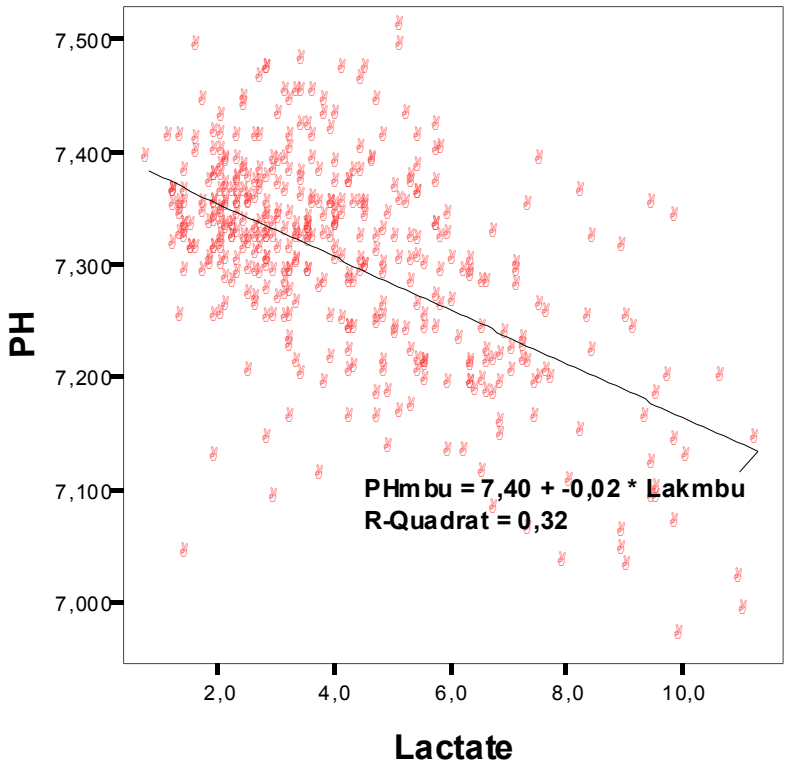
  $\Rightarrow lactate$

  $\Rightarrow BE$

- In the following 3 charts fig. ***B1, B2 and B3*** the last FSBA before delivery is taken and the correlation between foetal outcome and lactate (fig. B1), pH (fig. B2) and BE (fig. B3), is shown.

- To determine which lactate level assures a satisfactory foetal wellbeing, a TG-ROC technique devised by M. Greiner [34] was used. In fig. **"C",** Apgar 1 of more than 7, as a satisfactory outcome variable, and the lactate level of the last FSBA before delivery were calculated.

Fig. 6) *Fig A1: correlation of pH and lactate*



=> linear regression

Tab 6) correlations (pH – Lactate)

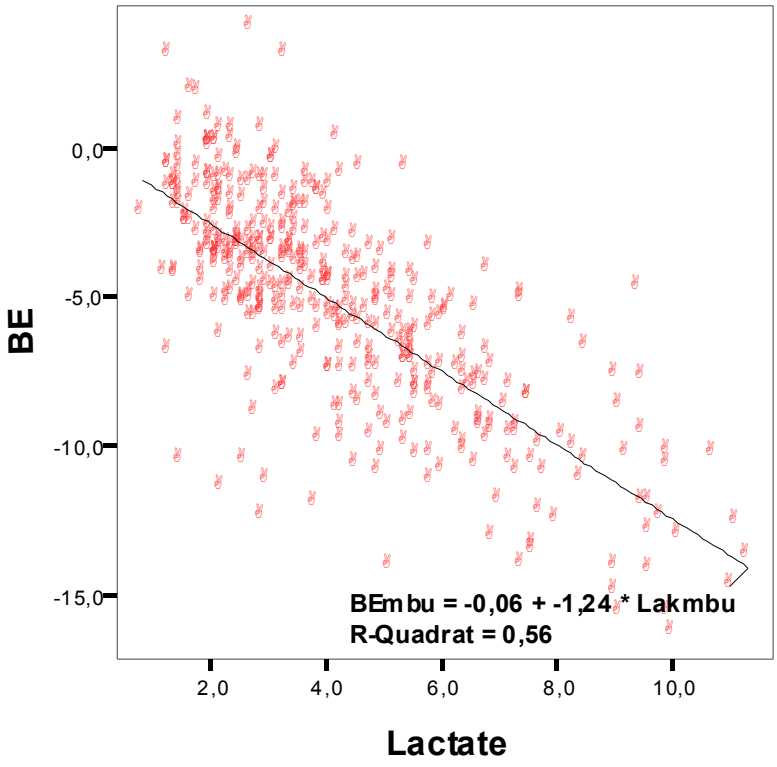
		Lact mbu	pH mbu
Lact mbu	correlation according to Pearson	1	-,565(**)
	significance (two-tailed)		,000
	N	414	414
pH mbu	correlation according to Pearson	-,565(**)	1
	significance (two-tailed)	,000	
	N	414	414

* The correlation is significant on a level of 0,01 (two-tailed).

A two-tailed $P < 0.05$ ($P = 0.01$) is considered statistically significant.

In this chart a clearly indirect proportional relationship between pH and lactate level is shown. As indicated in the fig. A1 it is significant, that newborns tended to have higher lactate levels when the pH level was low. The pH level is a common indicator for foetal asphyxia. The results above, show that lactate is as important as pH levels an indicator for foetal asphyxia.

Fig 7) *Fig A2: correlation of BE and lactate*



= linear regression

Tab 7) correlations (BE – Lactate)

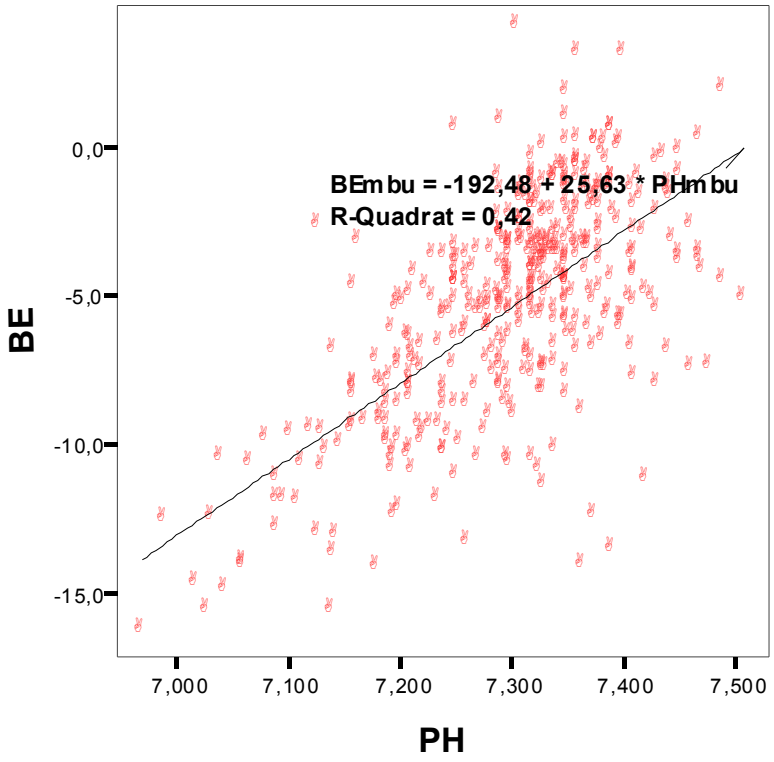
		Lakmbu	BEmbu
Lakmbu	correlation according to Pearson	1	-,748(**)
	significance (two-tailed)		,000
	N	414	412
BEmbu	correlation according to Pearson	-,748(**)	1
	significance (two-tailed)	,000	
	N	412	412

**The correlation is significant on the level of 0,01 (two-tailed).

A clearly indirect proportional relationship between BE and lactate values is shown in the chart above. It is clear to see, that newborns tended to have higher lactate levels when they had lower BE and this is also statistically significant ($P < 0.05$).

This result is expected, because BE represents the metabolic component of an acid-base disturbance.

Fig 8) *Fig A3: correlation of pH and BE*



Tab 8) correlations (BE – pH)

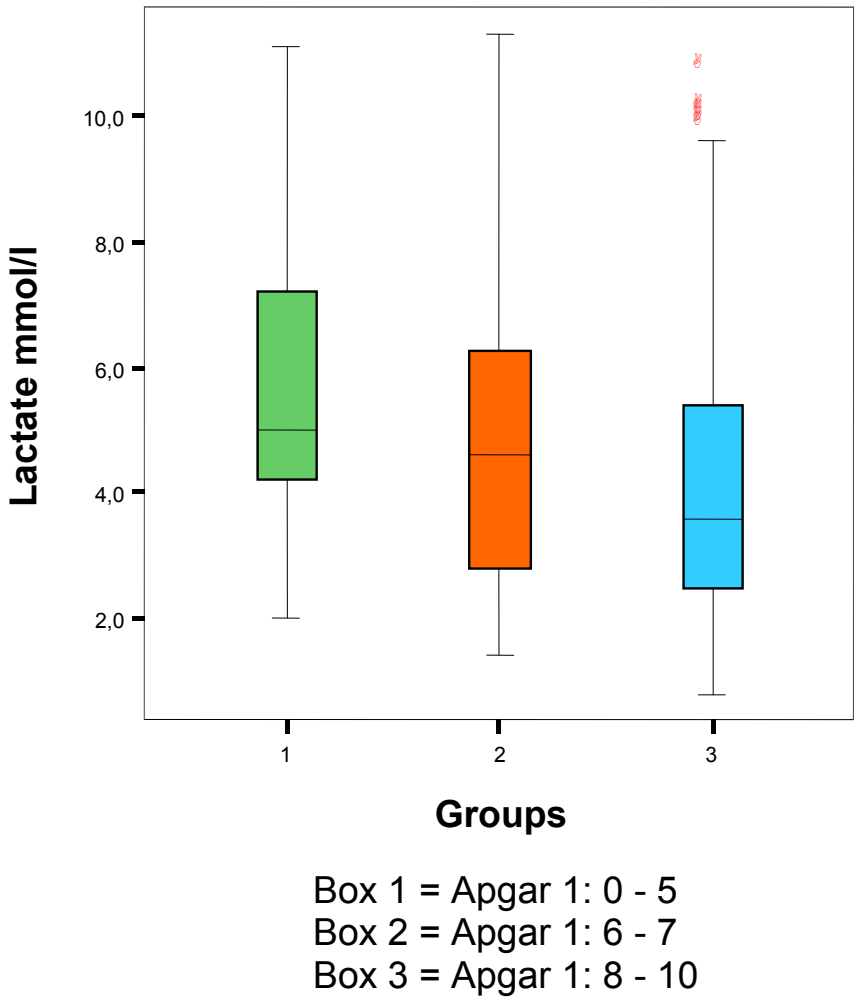
		BEmbu	PHmbu
BEmbu	correlation according to Pearson	1	,649(**)
	significance (two-tailed)		,000
	N	412	412
PHmbu	correlation according to Pearson	,649(**)	1
	significance (two-tailed)	,000	
	N	412	414

** The correlation is significant on the level of 0,01 (two-tailed).

A two-tailed $P < 0.05$ ($P = 0.01$) is considered statistically significant.

A clear direct proportional relationship between BE and pH levels is shown in the chart above. This result is also expected and a well known fact in the obstetrician's routine practice during labour. By diagnosing foetal blood sampling to assure infant wellbeing, the two variables, BE and pH, are common indicators for foetal asphyxia. In Fig.A3 the significant relationship is clearly shown.

Fig 9) *Fig B1: correlation of lactate and Apgar 1*

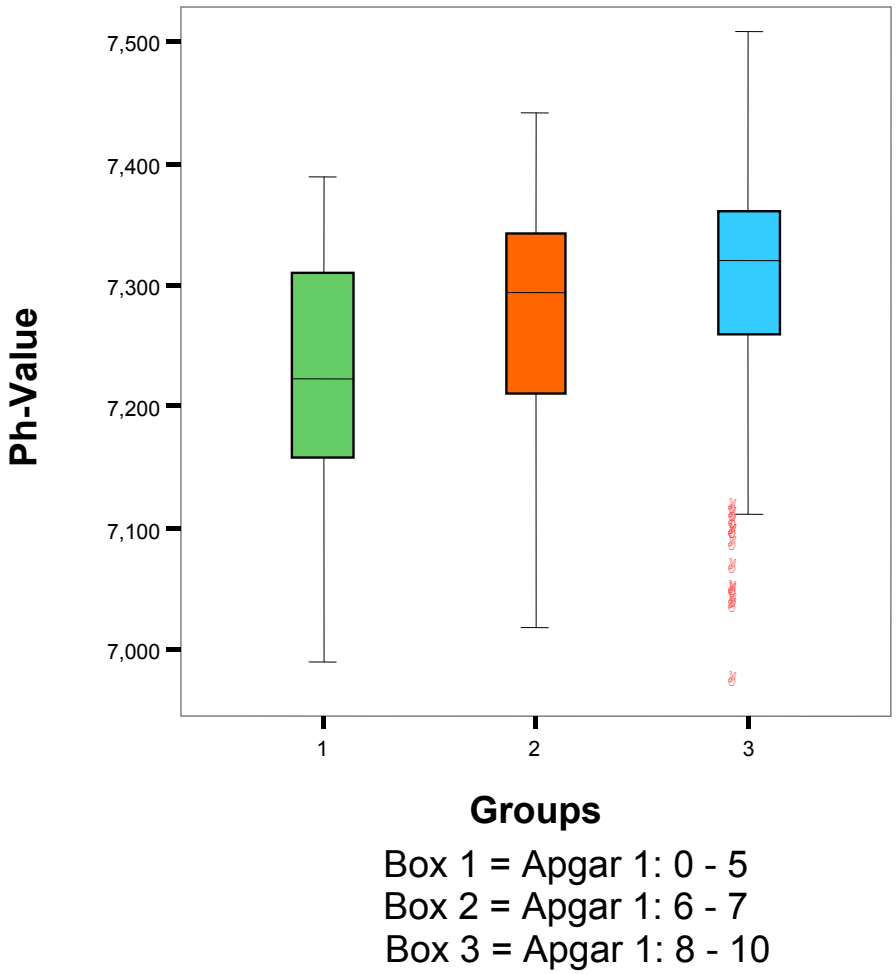


We divided the study cases into three groups to compare Apgar 1 outcome with lactate levels in the last FSBA before delivery.

1. Group (green) : all labours with Apgar 1 of 0-5 points
2. Group (red) : all labours with Apgar 1 of 6-7 points
3. Group (blue) : all labours with Apgar 1 of 8-10 points

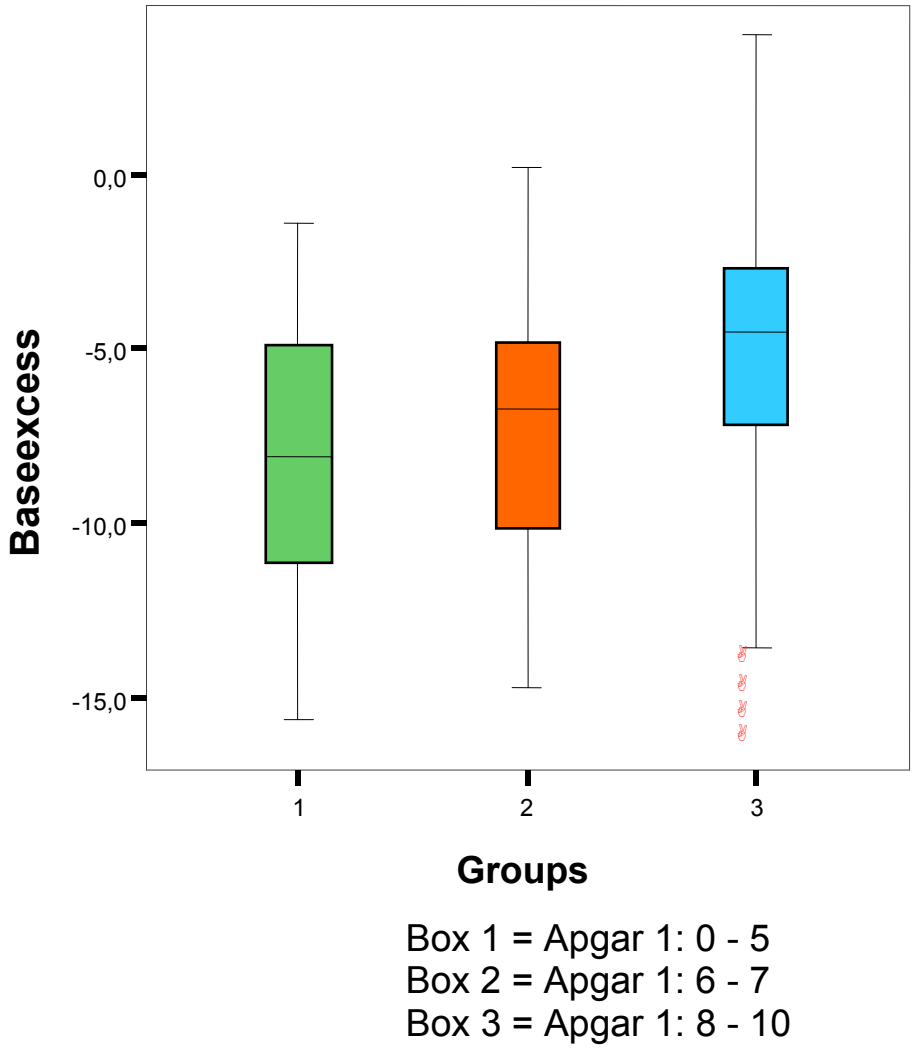
This shows clearly the difference of the lactate levels between the first group ("*Optimal group*") and the second group ("*Borderline group*") and the third group ("*Risk group*").
This chart shows an indirect relationship between Apgar 1 as a variable for foetal outcome and lactate level. Compared to infants with normal Apgar 1 (> = 8), infants with lower APGAR 1 tended to have higher lactate levels, nevertheless it did not reach significance.

Fig 10) *Fig B2: correlation of pH and Apgar 1*



The fig.B2 reveals a direct relationship between pH level and Apgar 1 as common indicator for foetal outcome. Compared to infants with normal APGAR 1 (> = 8), infants with low APGAR 1 tend to have also lower pH levels in foetal scalp blood analysis. The results shown in Fig. B1 and B2 suggest that lactate levels are equal to pH levels to define satisfactory foetal outcome.

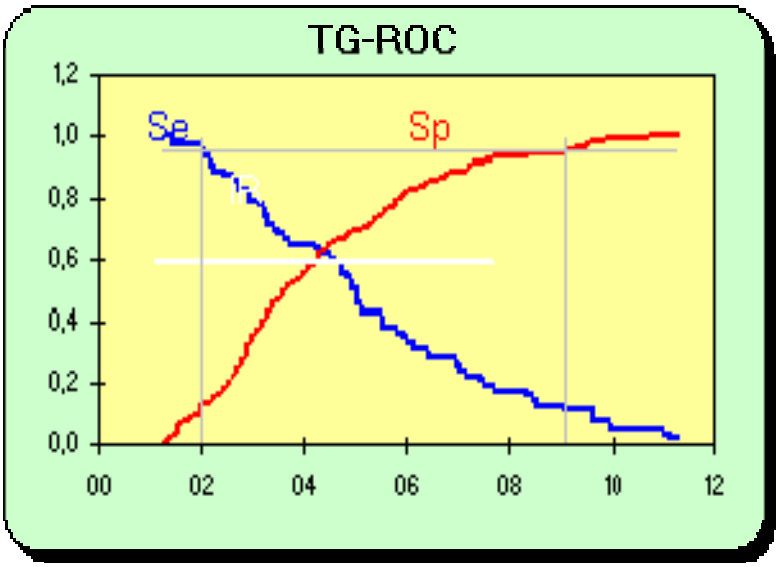
Fig 11) *Fig B3: correlation of base excess and Apgar 1*



This chart also shows a direct relationship between base excess and APGAR 1 as the well known predictor for foetal outcome again. Infants with lower APGAR 1 tend to have lower BE values in foetal scalp blood analysis, than infants with normal APGAR 1 (> = 8).
In addition to the distinct relationship of foetal outcome with pH and lactate levels, Fig. B3 illustrates the correlation between BE and foetal outcome. This variable, which is also determined by the FSBA, is a reliable indicator for a satisfactory foetal outcome, but not as clear as the pH and lactate-levels.

In summary, there is a distinct relationship of all three variables (pH, BE and lactate) to the foetal outcome.

Fig 12) *Fig C*



The objective of this analysis was to calculate a lactate level as cut – off level to assure *"Foetal wellbeing"*. "*Foetal wellbeing"* is defined by APGAR 1 score of not less than 7 (APGAR 1 = < 7).

TG-ROC designed by M. Greiner [34] analyses Apgar 1 as the main outcome variable, and the lactate level of the last FSBA before delivery.

In this analysis technique the most efficient level of lactate is derived by the intersection of the sensitivity and specificity curves for an APGAR 1 of = < 7.
The chart in the figure above predicts an APGAR 1 level of = < 7 at a lactate level of not more than 4.2 mmol/l.

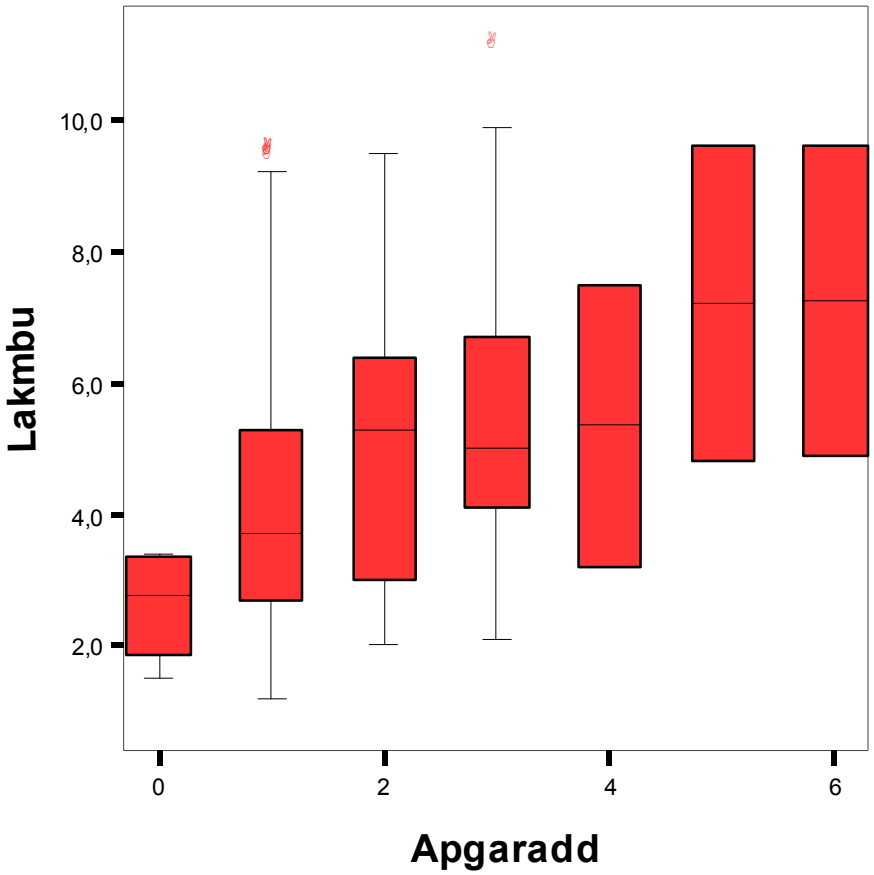
The non-pathological level of lactate is defined by 4.2 mmol/l. Rod M Allen et al. [35] established this result, which confirms the recommendation that a scalp lactate level of > = 4.2 mmol/l, or it's equivalent of a pH of < = 7.20, indicates that intervention is necessary to ensure neonatal wellbeing. Westgren et al. also confirmed this in a different study. [32]

However, a retrospective study of 1709 patients, Kruger et al. [33] established a scalp lactate level of 4.8 mmol/l which resulted in an intervention rate similar to that for a pH level of 7.20 [36]

It is important to point out that this indicative level of lactate in foetal scalp blood analysis should not be generalized.

Westgren *et al.*reported a FSBA failure rate of 1.3% of the lactate levels. This was compared with the 20.6%.examination failure rate of the pH levels. [8]

Fig. 13) *Fig D*



The difference of Apgar 5 and Apgar 1 values compared to lactate levels is shown in the chart above.

There is a direct proportional relationship between the two variables.

Conclusion:

The results suggest that increased lactate levels in foetal scalp blood analysis foetal lactacidosis are significantly linked to.

4. Discussion

Nowadays monitoring of infants during delivery with foetal scalp blood sampling is a common procedure to monitor foetal wellbeing to detect possible irregular heart rate pattern. Usually it is common to consider pH and BE results when deciding the next course of action. There is still discussion of including the lactate results in this decision-making process, but the matter is unresolved.

Our study shows the statistically significant correlation of pH and lactate levels and was further on able to confirm the widespread knowledge pertaining to correlation of pH and Apgar 1 as a variable for foetal outcome. A significant correlation between lactate level and Apgar 1 is evident. Based on this correlation, it is recommended to take the lactate and pH levels into account when determining the foetal wellbeing.

This is endorsed by a variety of studies, which have been published on the correlation of higher lactate-level and non-satisfactory foetal outcome.

As early as 1983, *A. Eguiluz et al.* established the mean foetal and maternal lactate levels in the three different stages of labour. They established a correlation between base excess and lactate levels. [37]

Lionel Dessolle et al. noticed that among elective caesarean sections lower lactate levels were evident than in any other forms of delivery. [31] This study supports our findings of increased lactate levels combined with an increased occurrence of asphyxia. The reason for the lower lactate levels in elective caesarean sections is that the uteroplacental perfusion is not compromised by uterine contractions and its not resulting in foetal distress.

Zhang Haiju et al. identified higher umbilical cord lactate levels during moderate-severe hypoxic ischemic encephalopathy than cases with mild hypoxic ischemic encephalopathy. A relationship between the lactate level and the degree of asphyxia was reconfirmed. [38]

The question of lactate being a better indicator of metabolic acidosis than pH should be addressed.

According to *Kerstin Krüger et al.* a significant correlation was evident between lactate concentrations in foetal scalp blood shortly before delivery and the lactate levels in the umbilical arterial and venous blood after delivery. Research shows that foetal lactate levels reveal more specific information about the degree of metabolic acidosis than the pH level. A pH level may fluctuate and causes unnecessary intervention.. This is based on the fact that respiratory acidosis in response to transient cord compression causes potential pH level fluctuations. [39]

There was an interesting publication of a similar study in 2004. For admission to the Neonatal Intensive Care Unit, *Rod M. Allen, et al.* established a lactate level of 4.1 mmol/l to predict an APGAR of < 7 at 1 min and for meconium stained liquor, and a lactate level of 4.2 mmol/l to predict an arterial cord pH of < 7.20. This study was based on 132 satisfactory samples (of 136 samples, 4 were unsuccessful) and our study included even more prenatal foetal scalp blood samples. [35]

It is important to mention the fact that delayed sampling results in increased lactate levels which is unreliable as it increases linearly with time regardless of the initial level and route of delivery. [31]

An increased lactate level is common during a) labour and especially during the second stage of delivery b) during acute ischemia, and remains elevated when ischemia becomes chronic. In order for the placenta to clear lactate level rapidly when the circulation is optimal, foetal lactate increases to a lesser extent than neonatal lactate. It is important to avoid sampling from badly circulated areas of the caput. A foetal scalp deformation and a limited circulation lead to an increased lactate level despite not compromising the foetus. An increased lactate level might also be induced by pressure of the amnioscope against the foetal head, which causes acute hypoperfusion. [35]

In a study in 2008, *Lionel Dessolle et al.* established the fact that lactate levels varied as did the sampling intervals. An increased lactate level was evident without occurrence of foetal hypoxia after delivery when arterial cord blood sampling was delayed. The lactate

level was always higher in the second sample than in the first. In Desolle's study, lactate levels increased linearly with time, by 0.062 mmol/l per min and depended on the initial lactate level and the route of delivery. Therefore cord blood sampling and lactate analysis should be performed immediately after delivery. [38]

These results do not affect on the results of our study, since we had taken this fact into account and determined the lactate levels accordingly.

It is important to mention that although there is no justification for the correlation in Diagram D, it is still of interest.

According to the results it is distinctly shown that lactate level combined with pH is an important factor for evaluating foetal wellbeing.

Foetal scalp blood analysis is an examination which can prevent a large number of unnecessary caesarean sections being performed, and furthermore reduce possible complications of maternal and foetal outcome. Under these circumstances, it is recommended to perform FSBA during labour in all hospitals to optimize foetal monitoring.

In order of this it is demonstrated that a lactate level of not more than 4.2 mmol/l is an indicator of a satisfying foetal outcome, which is defined as Apgar 1 =>7. This is also shown in the study of *Rod Allen et al.* in 2004, in which the lactate level also was derived of 4.2 mmol/l for their defined satisfying foetal outcomes.

We acknowledge that this study is a retrospective review of prospectively gathered data and not a true prospective study. However the high number of included patients is a strength of our investigation.

Conclusion

The lactate level in foetal scalp blood sampling is a significant indicator for foetal wellbeing and outcome. A lactate level of 4.2 mmol/l or greater is a clear indicator that the foetal wellbeing is non-satisfactory and a possible invention might be necessary.

5. References

[1] Brisbane, Todd. Childbirth in ancient Rome: from traditional folklore to obstetrics. Australian and New Zealand Journal of Obstetrics and Gynaecology 2007. 47. 82-85.

[2] Petru E, Schlembach D, Moser F, Häusler M, Lang U, Frudinger A, Mörtl M, Schoell W,Walcher W. Geburtshilfe-Skriptum. Servicebetrieb ÖH-Uni Graz GmbH Okt 2006. 5.Auflage

[3] James Drife. Clinical obstetrics and gynaecology ed. Edinburgh Saunders. 2007. 157-461.

[4] Riddle, John M. Contraception and Abortion: From the Ancient World to the Renaissance,.Cambridge: Harvard University Press. 1992. 7-15.

[5] Erich Saling - Institut für Perinatale Medizin (2009).
Bearbeitungsstand: 29. März 2008, URL: http://www.saling-institut.de (Abgerufen: 10. Dezember 2009, 16:52 UTC)

[6] Saling E. Neues Vorgehen zur Untersuchung des Kindes unter der Geburt-Einführung, Technik, Grundlagen. Arch Gynak. 1962. 197. 108-122.

[7] Hon EH. Instrumentations of foetal heart rate and foetal electrocardiography. II. A vaginal electrode. Am J Obstet Gynecol. 1963. 86. 772-84.

[8] Westgren M, Kuger K, Ek S, Grunevald C, Kublickas M, Naka K, et al. Lactate compared with pH analysis at foetal scalp blood sampling: a prospective randomised study. Br J Obstet Gynaecol 1998. 195. 29-33.

[9] Tuffnell D, Haw WL, Wilkinson K. How long does a foetal scalp blood sample take? BJOG. 2006. 113. 332-4.

[10] Wikipedia (2009).
Seite \'Obstetrics". Wikipedia, Die freie Enzyklop adie.
Bearbeitungsstand: 12. 10. 2009, 11:00 UTC.
URL: http://en.wikipedia.org/wiki/File:Scan12weeks.jpg (Abgerufen: 10.12. 2009, 21:02 UTC)

[11] GOOGLEbilder(2009).
Seite/http://images.google.at/intl/de_at/images/logos/images_logo.gif
URL: http://www.totgeburt.net/html/body_ctg.html
(Abgerufen: 10.12.2009, 20.07 UTC)

[12] Steven G. Gabbe, Jennifer R. Niebyl, Joe Leigh Simpson. Obstetrics- Normal and problem pregnacies, Churchhill Livingstone Elsevier. 2007. 386-387

[13] GOOGLEbilder(2009).
Seite/ http://images.google.at/images?gbv=2&hl=de&sa=3&q=foetal+scalp+blood
URL: http://www.nlm.nih.gov/medlineplus/ency/imagepages/9323.htm
(Abgerufen: 10.12.2009, 21:12 UTC)

[14] Maria J. Beckermann und Freiderike M. Perl. Frauen- Heilkunde und Geburts-Hilfe (Band2). Verlag Schwabe (Basel) 1. Auflage. 2004. 1299-1303.

[15] Goldaber KG, Gilstrap LC, Leveno KJ, Dags JS, McIntire DD. Pathologic foetal acidemia. Obstet Gynecol. 1991. 78. 11033-7.

[16] Low JA, Panagiotopolous C, Derrick EJ. Newborn complications after intrapartum asphyxia with metabolic acidosis in the term fetus. Am J Ostet Gynecol. 1994. 170. 1081-7.

[17] MacLennan A. A Template for defining a causal relation between acute intrapartum events and cerebral palsy: international consensus statement. BMJ. 1999. 319. 1054-9.

[18] Nordström. Baillieres. Foetal scalp and cord blood lactate. Best Practice Research in Clinical Obstetrics Gynaecology. 2004. 18. 467-76.

[19] IUPAC – The international Union of Pure and Applied Chemistry (2009).
Seite/ http:// www.**iupac**.org
Bearbeitungsstand: 8.Mai 2001,
URL:http://www.iupac.org/reports/provisional/abstract01/rondinini_prs.pdf
(Abgerufen: 12. Mai 2009, 21:38 UTC)

[20] Löffler. Basiswissen Biochemie mit Pathobiochemie (5. Aufl.). Berlin Heidelberg New York. Springer. 2002. S.106-149.

[21] Rainer Klinke und Stefan Silbernagl. Lehrbuch der Physiologie Thieme Verlag, 4. Auflage. 2003. Seite 217-287.

[22] Wikipedia (2009). Seite \Base-excess". Wikipedia, Die freie Enzyklopädie. Bearbeitungsstand: 01.. Dezember 2009, 22:18 UTC. URL: http://en.wikipedia.org/wiki/Base_excess (Abgerufen: 4. Dezember 2009, 9:16 UTC)

[23] Wikipedia (2009). Seite \PCO2". Wikipedia, Die freie Enzyklopädie. Bearbeitungsstand: 01.. Dezember 2009, 02:06 UTC. URL: http://en.wikipedia.org/wiki/PCO2 (Abgerufen: 4. Dezember 2009, 10:02 UTC)

[24] Dawes GS, Mott JC, Shelley HJ. The importance of cardiac glycogen for the maintenance of life in foetal lambs and newborn animals during anoxia. J Physiol. 1959. 146. 516-538.

[25] Shelley HJ. Glycogen reserves and their changes at birth. Br Med Bull. 1961. 17. 137-143.

[26] Greene KR, Green. Scalp blood gas analysis. Obstetrics Gynaecology Clinics of North America. 1999. 26(4). 641-643.

[27] Electronic obstetric data base - *"PIA"* - Hospital of Univ. Graz, 11.9.2009

[28] N Wiberg, K Källen, P Olofsson. Delayed umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations. BJOG An International Journal of Obstetrics and Gynaecology. 2008. 115(6). 697-703.

[29] Afschar P, Schöll W, Bader A, Bauer M, Winter R. A prospective randomised trial of atosiban versus hexoprenaline for acute tocolysis and intrauterine resuscitation. BJOG. 2004. 111(4). 316-8.

[30] Ramesh Agarwal, Ashish Jain, Ashok K. Deorari and Vinod K. Paul Post-resuscitation Management of Asphyxiated Neonates. Indian Journal of Pediatrics. 2008. 75 (2). 175-80.

[31] Lionel Dessolle, Jeremie Lebrec, Emile Darai. Impact of Delayed Arterial Cord Blood Sampling for Lactate Assay. A Prospective Observational Study Neonatology. 2008. 95 (3). 224-229.

[32] Westgren M, Kublickas M, Kruger K. The role of lactate measurements during labour. Obstet Gynecol. Surv. 1999. 54. 43-48.

[33] Shah S, Tracy M, Smyth J. Postnatal lactate as an early predictor of short-term outcome after intrapartum asphyxia. J Perinatol. 2004. 24. 16-20.

[34] 1996: Greiner M
Two-graph receiver operating characteristic (TG-ROC): update version supports optimisation of cut-off values that minimise overall misclassification costs.
Journal of immunological methods. 1996. 191(1). 93-4.

[35] Rod. M. Allen, Francis G. Bowling and Jeremy J.N. Oats. Determining the foetal scalp lactate level that indicates the need for intervention in labour. The Australian and New Zealand Journal of Obstetrics and Gynäcology. 2004. 44(6). 549-552.

[36] Kruger K, Westgren M. Reply to letters to the editor. Am J. Obstet Gynecol. 2000. 182. 1308.

[37] A. Eguiluz, A. Lopez Bernal, K. McPherson, J.J. Parilla, and L. Abad. The use of intrapartum foetal blood lactate measurements for the early diagnosis of foetal distress. American Journal of Obstetrics Gynaecology. 1983. 147 (8). 949-54.

[38] Zhang Haiju, Hao Suyuan, Fan Xiufang, Yang Lu and Ruopeng Sun. The combined detection of umbilical cord nucleated red blood cells and lactate: early prediction of neonatal hypoxic ischemic encephalopathy. Journal of perinatal medicine. 2008. 36(3). 240-7.

[39] Kerstin Krüger, MD, Marius Kublickas, MD, PhD, AND Magnus Westgren, MD, PhD. Lactate in Scalp and Cord Blood From Fetuses With Ominous Foetal Heart Rate Patterns. Obstet Gynecol. 1998. 92(6). 918-22.

Curriculum vitae

Persönl. Daten:

Name:	Natalie Fischer
Telefonnummer:	0043-664-4379564
Email Adresse:	NFischer1@gmx.at
Geboren:	10.08.1985 in Oberwart (Burgenland)
Hauptwohnsitz:	Plüddemanngasse 16/5/14 8010 Graz
Nebenwohnsitz:	Limbach 107 8241 Dechantskirchen
Religion:	röm.-kath.
Staatsbürgerschaft:	Österreich
Familienangehörige:	
Vater:	Ferdinand Fischer – ÖBB Beamter
Mutter:	Rosalinde Fischer - Bundesbedienstete
Schwester:	Sandra Fischer - Angestellte

Ausbildung:

- Volksschule 1991-1995
- Musikhauptschule (mit Klavierunterricht) 1995-1999
- Gymnasium
- (Musik Zweig mit Gesangsunterricht) 1999-2003
- Medizinische Universität Graz: 1. Abschnitt: 2003-2004
  2. Abschnitt: 2004-2008
  3. Abschnitt: ab 2008

Sonderstudienmodule:

- Klinische Humangenetik
- Chirurgische Operationslehre - von der Therapie zur Praxis
- Klinisch-topografische Anatomie der Eingeweide
- Klinisch-topografische Anatomie der Extremitäten
- Angewandte Physiologie

Bisherige Famulaturen:

2005: 4 Wochen internistische Abteilung LKH Hartberg
2006: 3 Wochen chirurgische Abteilung LKH Hartberg
2007: 4 Wochen chirurgische Abteilung St. Anna Hospital Ferrara (Italien)
2008: 2 Wochen Dr.med. Gottfried Thalhammer (allg. medizinische Praxis)
8 Wochen internistische Abteilung Universitätsspital Zürich (Schweiz)
2009: 4 Wochen Alpine Kinderklinik Davos (Schweiz)

Zusätzliche medizinische Ausbildungen:

- Rotes Kreuz Graz (seit Jänner 2005)
- Rettungssanitäter (seit Dezember 2005)

Zusätzliche Ausbildungen:

- B-Führerschein (2002 / L17-Ausbildung)
- Peer-Education zum Thema Gewalt (Kinderschutzzentrum Graz)
- ECDL Computerführerschein
- Angestellte – Bar/Restaurant Schillerhof (Schillerplatz 1, Graz)
- seit April 2008
- Ausbildung zur Kinderanimateurin (*Käpt`n Hugo*, Sommer 2008)

Sprachkenntnisse:

Englisch fließend in Wort und Schrift
Italienisch (Grundkenntnisse)

Hobbys, Interessen:

Sport: Laufen, Klettern, Mountainbiken
Musik: Klavierunterricht: 1993-2002
Gesangsunterricht: 1999-2003
Mitgestaltung eines Musicals
Reisen: Schwerpunkt europäische Hauptstädte
Lesen