Acute reduction of uterine blood flow and fetal heart rate changes in pregnant sheep near term

Heinz-Dieter Junge, Wolfgang Künzel, Friedrich Karl Klöck

Universitäts-Frauenklinik Würzburg (Head: Prof. Dr. K.-H. Wulf)

Frauenklinik der RWTH Aachen (Head: Prof. Dr. H. Jung)

Vigorous uterine contractions may be the cause of repetitive acute reductions of uterine blood flow (UBF) (Fig. 1) [1, 2, 6, 8, 15, 23, 33] and the cause of decelerations of the fetal heart rate (FHR). Although this fact is of great interest for the evaluation of FHR recordings during parturition little is known about quantitative aspects. ASSALI et al. [3] reported a FHR decrease (= deceleration amplitude) of 10 bpm with a 25% reduction of UBF, a deceleration of 20 bpm with a 50% reduction of UBF and a deceleration of 68 bpm with a 90% reduction of UBF (Mean values) in fetal lambs in utero. Basal UBF and basal FHR prior to UBF reduction were not taken into consideration. Yet it is known that there is a decrease in basal UBF in chronic and subchronic uteroplacental insufficiency in man [9]. So we were interested to reevaluate the quantitative relationships between basal UBF, basal FHR, the amount of acute repetitive UBF reduction and FHR changes.
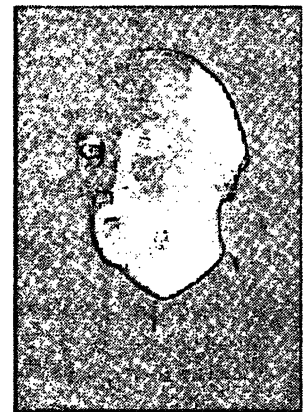
Curriculum vitae

HEINZ-DIETER JUNGE, M.D. Born in Kiel, 1935. Studying Medicine at the University of Kiel. 1963–1969 Staff member, Department of Obstetrics and Gynecology, University of Kiel. In 1969 taking a and Computer Technique at the Bioelectronic and Computer Labs of the Cardiologic Branch, Pediatric Department, University of Kiel on a grant of the "Stiftung Volkswagenwerk". 1970–1973 Staff member, Department of Obstetrics and Gynecology, Medizinische Hochschule Hannover. Since 1973 Lecturer (Privatdozent), Department of Obstetrics and Gynecology, University of Würzburg. Fields of interest: Technical and clinical aspects of cardiotocography, fetal cardiovascular regulation and state of arousal. Main present interest: Computer aided CTG-Monitor-Systems (CMS).

1 Material and methods (Fig. 2)

1.1 Five merino sheep near term were used for acute preparations. Maternal weight was 66,6 kg (Mean). Mean fetal weight was 4,2 kg. Three sheep had a single fetus and two had twin fetuses.

1.2 For recording and later evaluation of signals a multi-channel pen recorder (Hellige) and a multi-channel analog tape (Philips) were used. Calibration of heart rate meters with a function generator and of electro-manometers with a Hg-manometer was performed before the beginning and after the end of each experiment. Preliminary calibration of the flow meter was achieved by running definite amounts of NaCl-solution per time through a catheter fitted into the flow meter cup. For definite calibration this procedure was repeated at the end

SHEEP No. 20

t (min)

INTRAUTERINE PRESSURE (mmHg)

40
20
0

UTERINE BLOOD FLOW (ml/min)
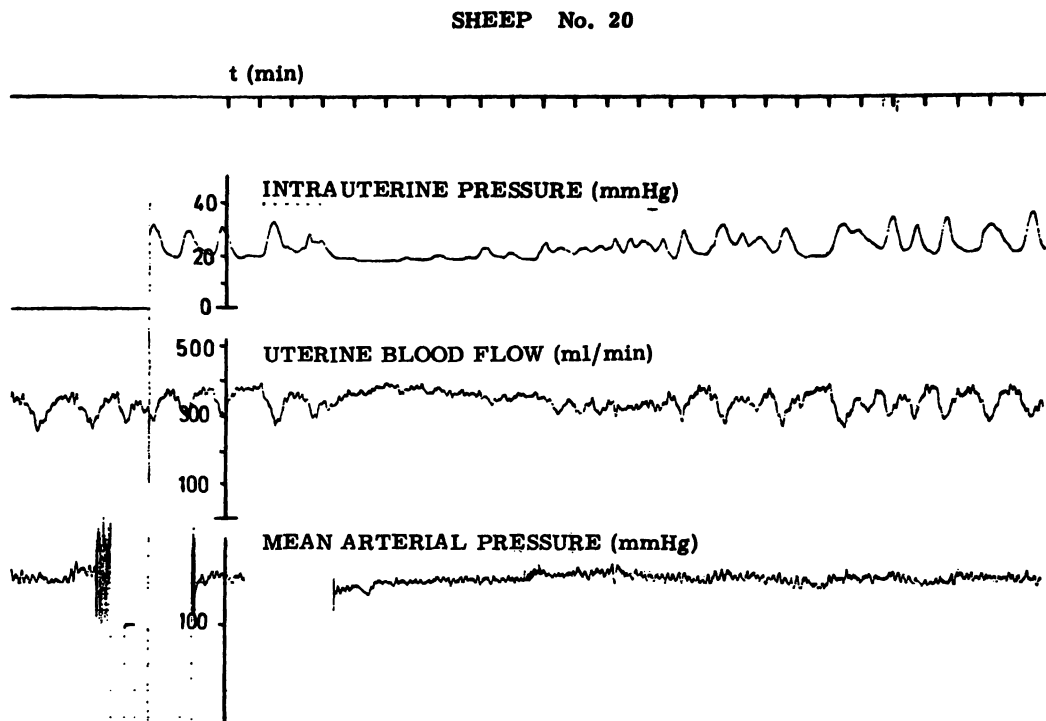
500
300
100

MEAN ARTERIAL PRESSURE (mmHg)

100

Fig. 1. Simultaneous recording of intrauterine pressure, uterine blood flow and mean arterial pressure in a pregnant sheep. Contraction elicited decreases in uterine blood flow can be seen clearly.

V. uterina

A. umbilicalis

V. umbilicalis

V. jugularis

Pentobarbital
5 mg/kg/h

Uterus

A. brachialis
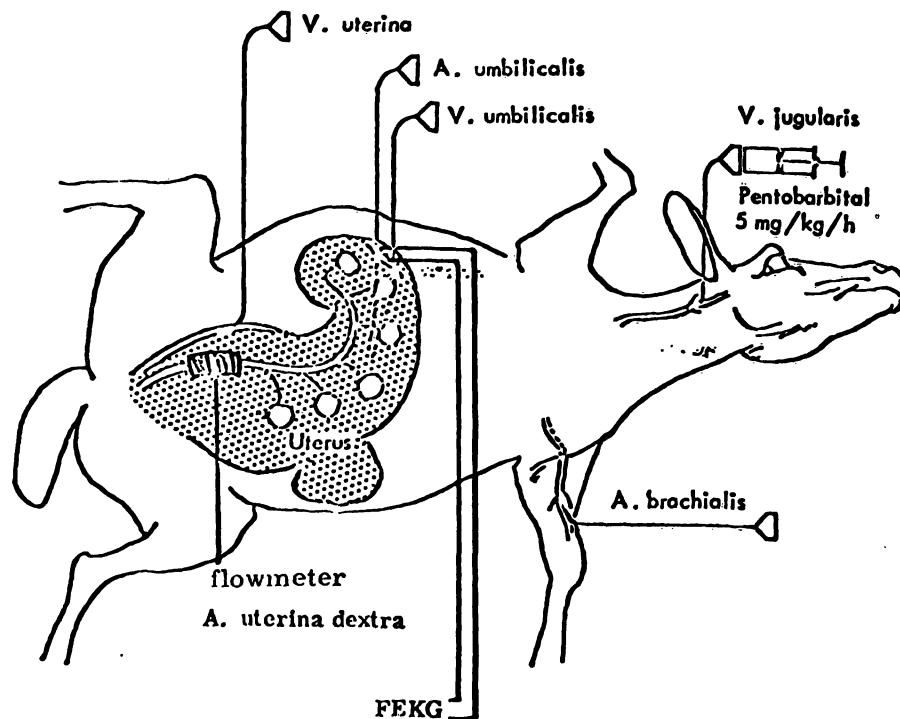
flowmeter
A. uterina dextra

FEKG

Fig. 2. Diagram showing the experimental set up.

of each experiment using the ewes' own blood running from the carotid artery.

1.3 The ewes were anaesthezised with pento-barbital (initial dose 20 mg/kg i.v., continued by infusion of 5 mg/kg/h) and Alloferin was given for relaxation. The ewe was then placed on a surgical table in left lateral position. After tracheotomia intubation was performed and ventilation was maintained by a Starling pump. Electrodes were attached to the maternal chest for recording maternal ECG and heart rate. Polyethylene tubes were inserted into the jugular vein for administering the anaesthetic and into the brachial artery for recording arterial pressure via a pressure transducer. The abdominal wall was opened by a right lateral section and the uterine horn containing the fetus was partially exposed. First of all thin catheters were inserted into branches of the umbilical artery and umbilical vein through small incisions of the uterine wall leaving the amnion intact. Fetal ECG and FHR were recorded via very thin, partially unisolated platinum wires inserted subcutaneously into the fetal back by puncturing the uterine wall and the fetal skin with a long puncture needle. Another catheter was inserted into the uterine cavity by puncturing its wall for recording in-trauterine pressure. Both uterine arteries were freed from surrounding tissues after infiltration with local anaesthetics to prevent spasm. Firstly the artery of the gravid horn was inserted into the cage of the flow meter cup and blood flow was

recorded for some time. The measurement was taken valid when blood flow was stable. Then the flow meter cup was put around the artery of the other side and blood flow was measured in the same way. Both measurements were added and taken as total uterine blood flow. At last the flow meter cup was put back around the artery of the gravid horn again and then the abdominal wall was closed. Now the calibration scale of the blood flow channel was corrected according to the initial ratio of flows in both uterine arteries presuming that this ratio would remain constant throughout the course of the experiment.

1.4 Blood samples drawn form the catheters were kept in glass capillaries at low temperature until analyses of pO_2, pCO_2, and pH were performed. These were done with an Eschweiler appartus.

1.5 Investigationson UBF reduction and fetal response were started at various times after initial surgical preparation depending on our program of several items being investigated in each preparation. At that time different degrees of deterioration of the ewes and hence the fetuses were seen but this was in agreement with our experimental intentions. Repetitive and progressive acute reduction of UBF (approximately 25%, 50% and 100% from basal UBF value) was achieved three times, lasting 120 sec each and each approximatly 12 min apart, by flowmeter controlled partial or total occlusion of the aorta abdominalis of the ewe with a balloon
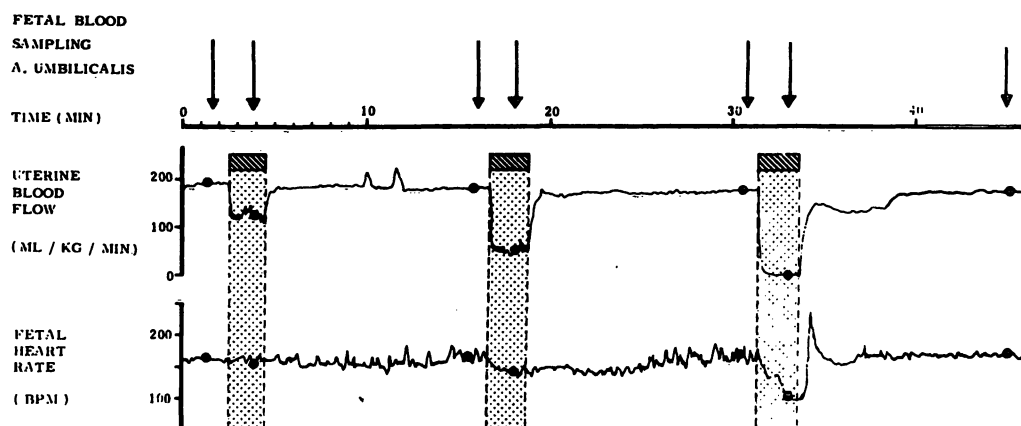

Fig. 3. Semischematic diagram showing data aquisition during repetitive acute flowmeter controlled reduction of uterine blood flow.
Blood sampling was performed discontinuously (arrows). Simultaneous data of UBF and FHR were taken from continuous recordings (black dots).

catheter inserted into the aorta. (In some cases the lateral abdominal section was left open and the aorta was compressed manually).

Before, 90 sec after the beginning and 10 min after the end of UBF reduction blood samples were taken from the fetal catheters (Fig. 3). In two preparations this sequence was repeated once after complete recovery of FHR.

2. Results

Data of all fetuses and all UBF reduction sequences are given in Table I and Fig. 4.

2.1 Data before and after UBF reduction sequence

Initial UBF values ranged from 180 to 57 ml/kg/min (Mean 104.0, SD ± 37.5 ml/kg/min). Thus situations with physiologic avlues of UBF, borderline situations

Fig. 4. Mean values of UBF, pO_2, pCO_2 and pH in the umbilical artery as well as FHR for all 7 UBF reduction sequences performed. (Arrows in upper part indicate UBF reduction).

and situations with extremely pathologic UBF values could be investigated, which was in agreement with our experimental intentions.

PO_2 in the umbilical artery ranged from 18.5 to 6 Torr (Mean 13.3, SD ± 5.1 Torr), indicating moderate to severe fetal hypoxemia. Overall there was a combination of high UBF values with high pO_2 values and vice versa, but correlation was not significant r = .42, 2 $\alpha <$ .1).

PCO_2 in the umbilical artery was in the range of 37 to 57 Torr (Mean 44.9, SD ± 6,7 Torr). No significant correlation to UBF could be found. PH in the umbilical artery ranged from 7.43 to 7,23 pH units (Mean 7.34, SD ± .06 pH units) and there was no correlation to UBF.

FHR ranged from 130 to 235 bpm (Mean 186.4, SD ± 34 bpm). Thus a wide range of fetal cardiovascular situations was under investigation too. Except preparation No. 20 there was in inverse relationship between basal UBF and FHR (r = − .48, 2$\alpha <$ .05) and an inverse relationship between basal pO_2 and FHR (r = − .46, 2$\alpha <$ .05). Altogether low basal UBF was accompanied by fetal hypoxemia and tachycardia (Figs. 5 and 6).

2.2 Ten minutes after the whole UBF reduction sequence mean values for UBF and pO_2 were not altered in comparison to initial values, pCO_2 was elevated by 9.7 Torr, pH was lowered by .13 pH units. FHR had increased by 48.6 to 225 bpm.

2.3 Relationship between acute reduction of of UBF (ΔQ_{UT}) and FHR decrease (ΔFHR = deceleration amplitude).

The scattergram of ΔFHR versus ΔQ_{UT} prima vista does not show any relationship (Fig. 7). But transformation of the scattergram by taking ΔFHR and ΔQ_{UT} as percentage of basal values gives good results (Fig. 8). (100 bpm was defined as $\emptyset$ % of basal FHR value because with 100% reduction of UBF heart rate of the fetal lamb decreased to about 100 bpm (Mean 104.2, SD ± 10.5 bpm)). In fact an alinear correlation can be seen. This fact must lead to the conclusion that $\Delta FHR/\Delta Q_{UT}$ is dependent on basal UBF and FHR levels. In order to prove this the $\Delta FHR/\Delta$ A_{UT} were plotted versus basal UBF (Fig. 9) and basal FHR (Fig. 10). A significant alinear correlation can be found for both. Relations are inverse because of the inverse
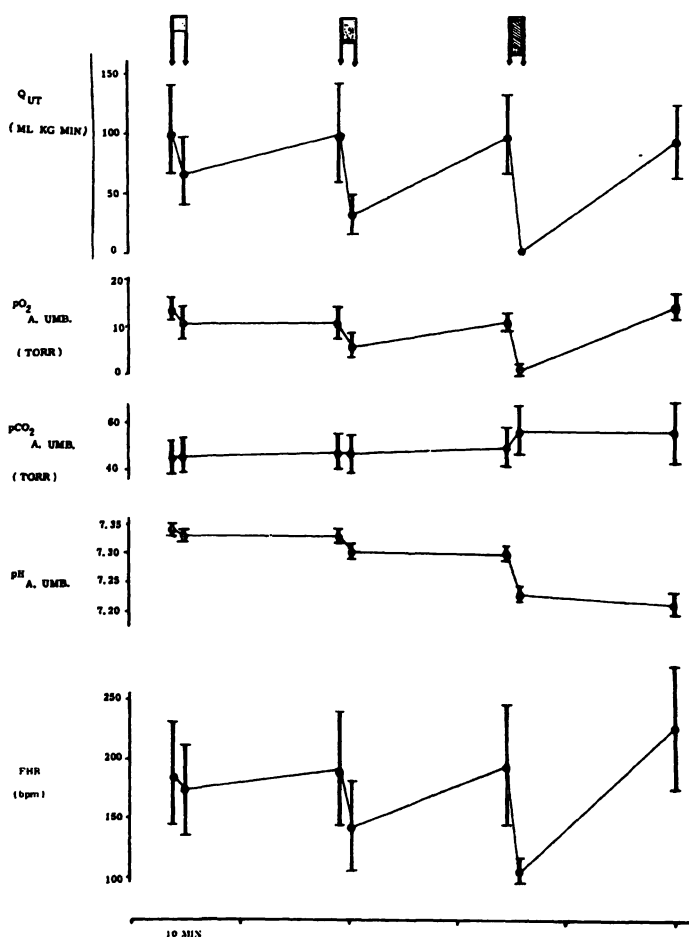
Tab. I. Data for UBF (Q_{ut}, ml · KG⁻¹ · min⁻¹), FHR (bpm), pH (pH – units), pCO_2 (Torr) and pO_2 (Torr) before, 90 sec after the onset and 10 min after the end of approximately 25%, 50% and 100% UBF reduction.

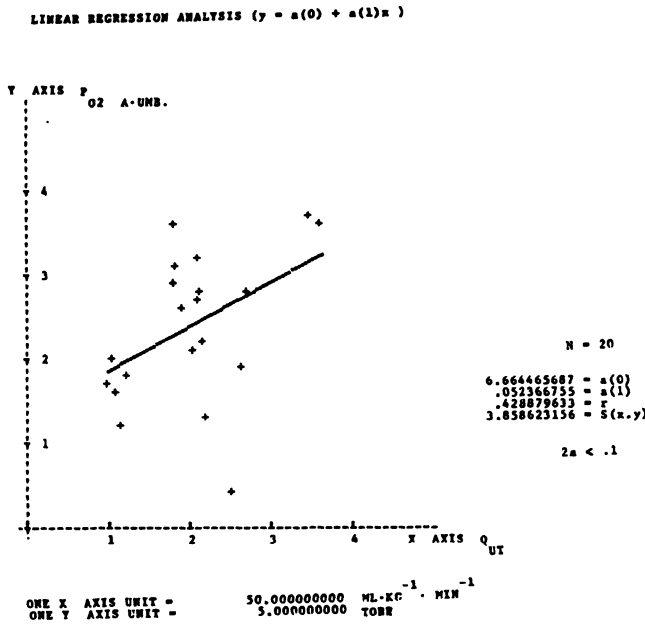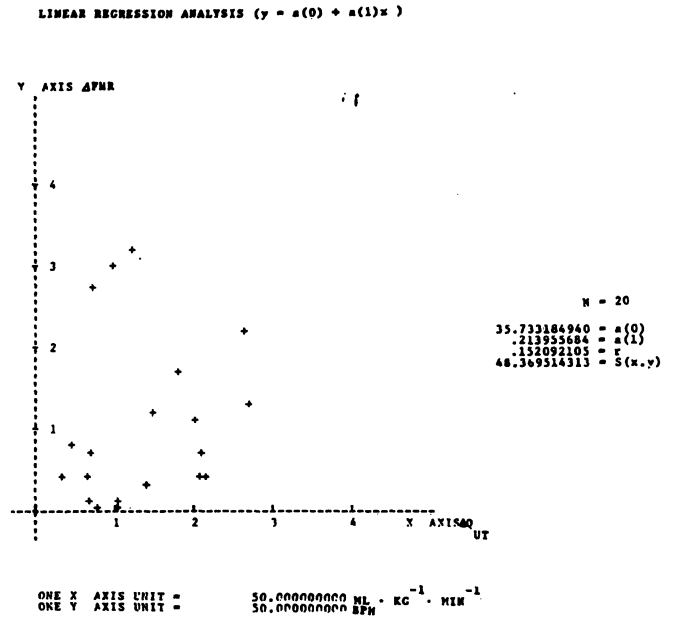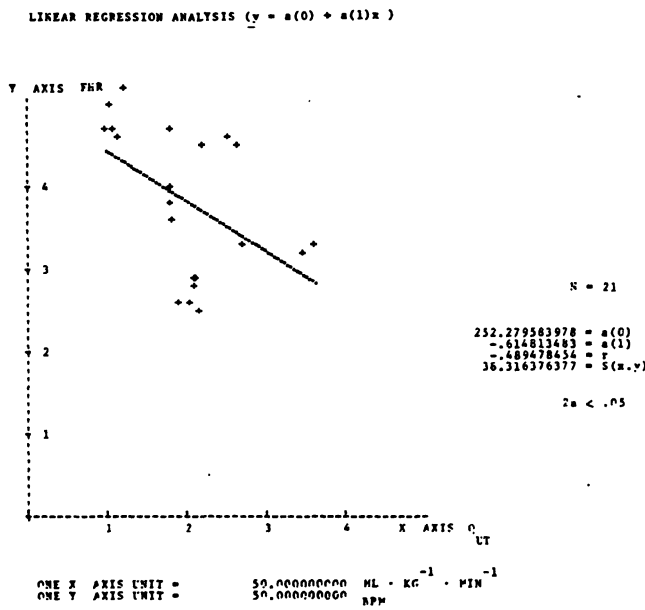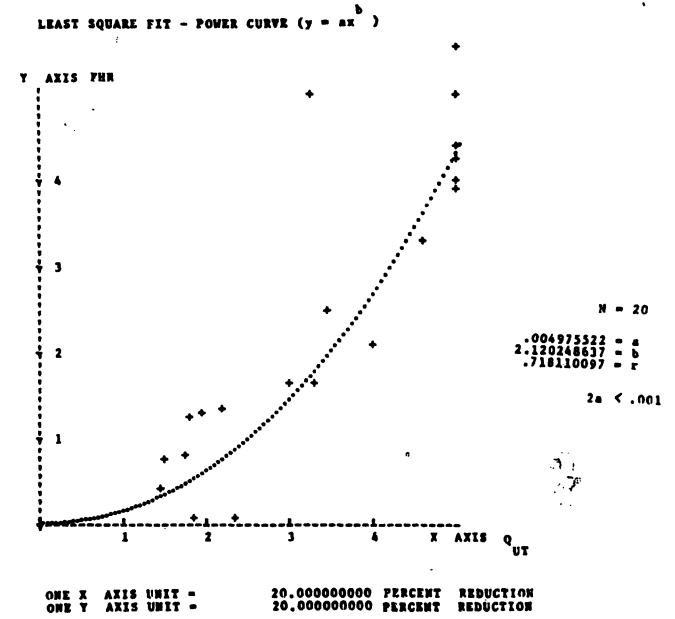| sheep Nr.	Q_{ut} before	Q_{ut} during	Q_{ut} after	FHR before	FHR during	FHR after	pH before	pH during	pH after	pCO_2 before	pCO_2 during	pCO_2 after	pO_2 before	pO_2 during	pO_2 after
11	110	58	126	225	225	250	7.30	7.29	7.32	57	54.5	55	6.5	2	2
	126	25	132	230	175	225	7.32	7.29	7.29	55	33.5	55.5	2	0	9.5
	132	0	107	225	115	250	7.29	7.22	7.21	55.5	45	51.5	9.5	0.5	10.5
15	91	58	90	180	160	190	7.43	7.45	7.40	37	37	40	15.5	14	12.5
	90	16	90	190	130	200	7.40	7.34	7.40	40	47	39	14.5	17	12
	90	0	86	200	115	275	7.40	7.34	7.34	39	45.5	44	18	5	14.5
16	90	55	52	235	200	250	7.38	7.36	7.34	45	47.5	44	18.5	14.5	10
	52	29	61	250	210	260	7.34	7.32	7.23	44	47	48	10	10	9
	61	0	63	260	100	275	7.32	7.25	7.28	48	52.5	52	9	7	15.5
	180	128	173	165	160	160	7.34	7.39	7.36	43.5	47	50.5	18	17.5	18.5
	175	69	135	160	140	165	7.36	7.37	7.35	50.5	49.5	52	18.5	10	14
	135	0	135	165	100	245	7.35	7.31	7.33	52	57	53.5	14	1	20.5
17	57	40	54	230	210	235	7.23	7.15	7.13	49.5	57	54.5	6	4	8
	54	19	49	235	98	235	7.13	7.11	7.06	54.5	60	61	8	2	8.5
	49	0	46	235	85	220	7.06	6.99	6.82	61	72	85	8.5	2.5	5.5
20	95	61	102	130	125	130	7.37	7.37	7.38	44	47.5	47.5	13	10.5	10.5
	102	32	108	130	115	125	7.38	7.36	7.32	47.5	49	47	10.5	5	11
	108	0	105	125	105	150	7.32	7.25	7.28	47	63	53	11	0	10.5
	105	67	106	140	140	145	7.34	7.34	7.37	38.5	37	36	16	14	14
	106	36	105	145	130	145	7.37	7.35	7.35	36	41.5	40	14	6	13.5
	105	0	105	145	110	160	7.35	7.24	7.22	40	56	46	15.5	1	14

Fig. 5

Fig. 7

Fig. 6

Fig. 8

Fig. 5. Relationship between basal pO_2 in the umbilical artery and basal UBF (Q_{UT}) prior to each UBF reduction.

Fig. 6. Relationship between basal FHR and basal UBF (Q_{UT}) prior to each UBF reduction.

Fig. 7. Scattergram of values of ΔFHR versus ΔQ_{UT}. No relationship for ungrouped values.

Fig. 8. Significant alinear correlation between ΔFHR and ΔQ_{UT}, both taken as percentage of basal values. (100 bpm was defined as $\emptyset\%$ of basal FHR value, because with 100% UBF reduction the lowest FHR seen was about 100 bpm).
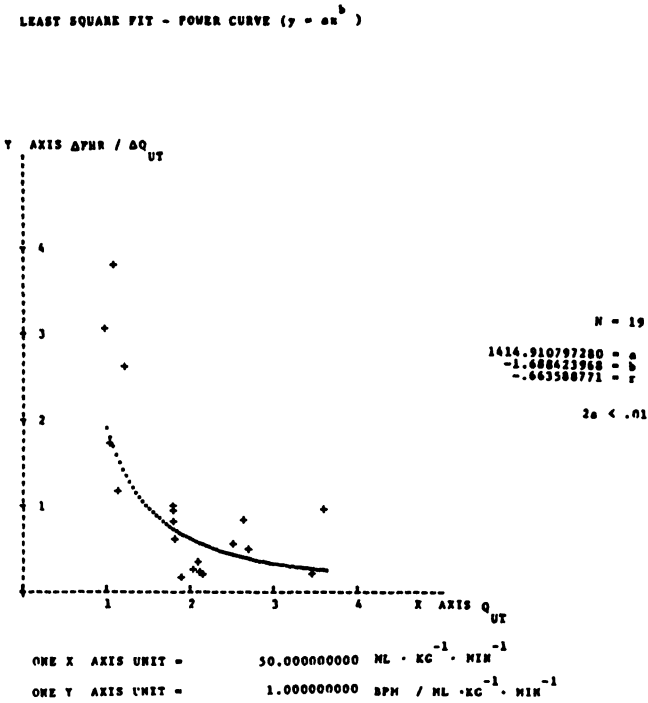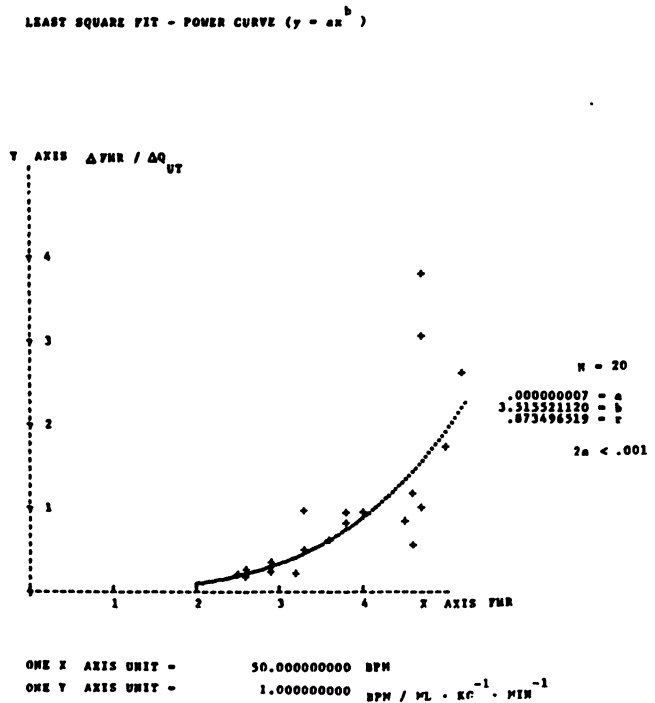
LEAST SQUARE FIT - POWER CURVE (y = ax^b)

Fig. 9

Fig. 10

Fig. 9. Significant alinear correlation between ΔFHR/ΔQ_{UT} ratio and basal UBF (Q_{UT}). Deceleration amplitude per unit of UBF decrease rises sharply when basal UBF is below 100 ml/kg/min.

Fig. 10 Significant alinear correlation between ΔFHR/ΔQ_{UT} ratio and basal FHR. Deceleration amplitude per unit of UBF decrease rises sharply when basal FHR is elevated to its maximum.

relationship between basal UBF and basal FHR (see above).

Reevaluation of the scattergram of ΔFHR versus ΔQ_{UT} anew by grouping data according to normal, prepathologic and pathologic basal levels of Q_{UT} (Fig. 11) and FHR (Fig. 12) gives sense now. Using the least square fit power curve (y = ax^b) statistically significant alinear regression lines for the physiologic range of basal UBF (Q_{UT} > 100 ml/kg/min) and the physiologic range of basal FHR (FHR < 170 bpm) may be fitted. For the intermediate and pathologic ranges alinearity is not statistically significant but because of the alinearity in the percentage regression (see Fig. 6) which includes all data, alinear regressions for the intermediate and pathologic ranges were calculated too.

From this the following conclusions may be valid: Within physiologic levels of UBF and FHR minor and moderate acute reductions of UBF do not affect FHR at all or lead to minor decelerations.

Only a substantial reduction will cause decelerations of larger amplitude. But with decreasing basal UBF levels (and increasing FHR levels) the same absolute amount of UBF reduction leads to increasing deceleration amplitudes.

2.4 It is a widely accepted opinion that FHR decelerations caused by acute UBF reduction are mediated by a fall in fetal pO_2 via vagal stimulation and/or direct depression of the heart. Therefore it seemed interesting to evaluate relations between UBF and pO_2 alterations as well as the relations between pO_2 and FHR alterations.

2.4.1 Relationship between acute reduction of UBF (ΔQ_{UT}) and change of pO_2 in the umbilical artery (ΔpO_2) during moderate to severe fetal hypoxemia.

Ninety seconds after the start of acute UBF decrease pO_2 in the umbilical artery had fallen (Range 0 to 13 Torr, Mean 6.45, SD ± 4.5 Torr). A statistically
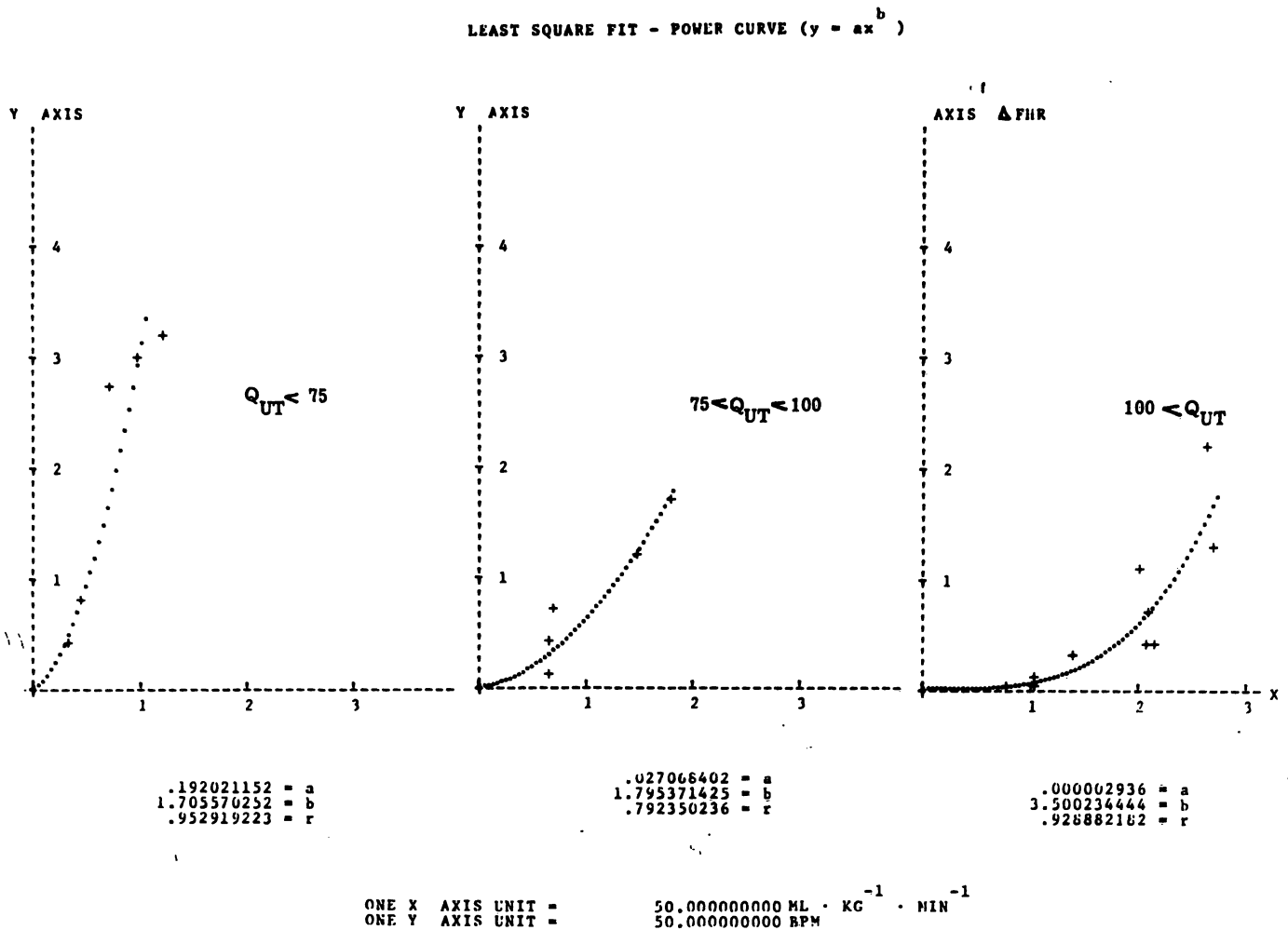
LEAST SQUARE FIT - POWER CURVE $(y = ax^b)$

Fig. 11. Relationship between absolute values of ΔFHR and ΔQ_{UT} for physiologic (graph on the right), prepathologic (graph in the center) and pathologic (graph on the left) levels of basal UBF. Significant alinear correlation for ΔFHR versus ΔQ_{UT} and basal $Q_{UT} > 100$ ml/kg/min. Alinearity not significant for basal $Q_{UT} < 100$ ml/kg/min, but the slope of regression is rising with falling basal Q_{UT}.

highly significant linear correlation exists between decrease of UBF and decrease of pO_2 ($r = .80$, $2\alpha < .001$) (Fig. 13). The regression may be approximated by $\Delta pO_2 = .1 \Delta Q_{UT}$, i.e. a UBF reduction of 50 ml/kg/min will on an average lead to a pO_2 decrease of 5 Torr.

2.4.2 Relationship between acute fall of pO_2 in the umbilical artery (ΔpO_2) and FHR decrease (ΔFHR), the deceleration amplitude.

Correlation between ΔQ_{UT} and ΔpO_2 being linear and highly significant the same relation between ΔFHR and ΔpO_2 should be expected as between ΔFHR and ΔQ_{UT}. This holds true in general: a significant correlation between the ΔFHR/ΔpO_2 ratio on basal FHR can be seen, but the ΔFHR/

ΔpO_2 ratio is not well correlated to basal pO_2 and alinearity for the regression of ΔFHR on ΔpO_2 in the normal FHR range could not be verified statistically. A linear regression was found significant for this range as well as for the range of severe tachycardia. For moderate tachycardia no significant correlation could be verified (Figs. 14–17).

2.5 Lag time of UBF reduction induced FHR fall

A histogram of lag times between the onset of UBF reduction and onset of FHR fall is shown in Fig. 18. It can be seen that the lag time was less than 11 sec in about 40% and less than 21 sec in about 80%. A correlation between basal FHR level and lag time could not be verified.
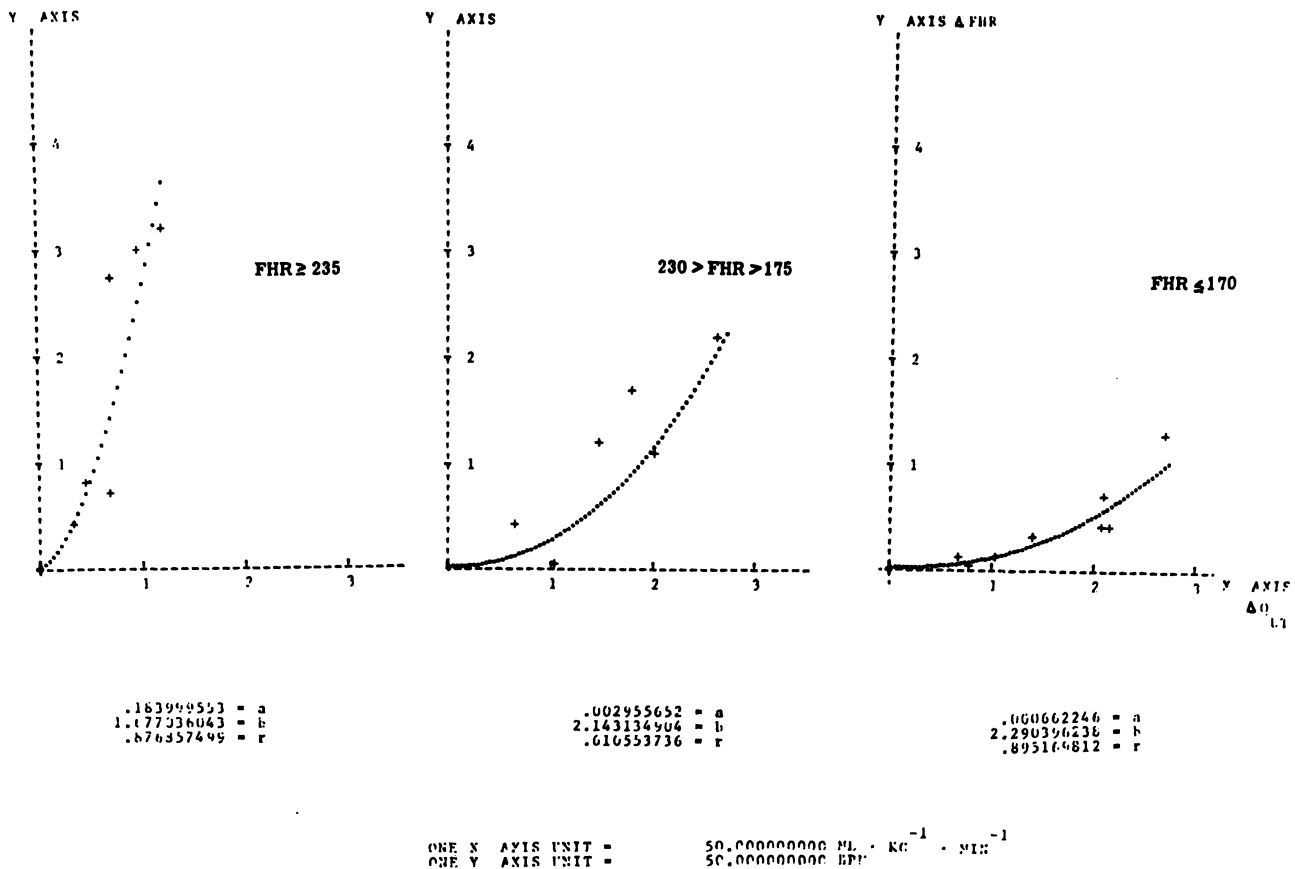
Fig. 12. Relationship between absolute values of ΔFHR and ΔQ_UT for various levels of basal FHR. The slope of regression is rising with rising level of basal FHR.

3. Discussion

All obstetricians practicing FHR monitoring are confronted with the problems of correct interpretation of FHR recordings. A late deceleration pattern is commonly taken as a sign of developing fetal distress and severeness of decelerations and fetal distress is judged in part from deceleration amplitudes. But there is little information about factors influencing deceleration amplitude. ASSALI and coworkers [3] published data on the relationship between reduction of UBF and FHR decrease. Our present data give additional knowledge concerning the influence of basal UBF and basal FHR and the role of the UBF reduction induced fall of fetal pO_2, which is supposed to mediate the fall of FHR.

First of all a discussion of the time courses of UBF, pO_2 and pH in the umbilical artery and of FHR in connection with repetitive acute reduction of aortic flow and hence UBF is worth while (Fig. 4).

3.1 UBF dropped rapidly on reducing blood flow in the lower aorta of the ewe. On deflation of the obstructing balloon catheter UBF rose as rapidly again, but on 50% to 100% reduction this rise was sometimes followed by a slight rebound fall that gradually faded out. This phenomenon will be discussed on below.

3.2 Mean pO_2 in the umbilical artery – initially in the moderate to severe hypoxemic level – fell rapidly and proportionally to the amount of UBF
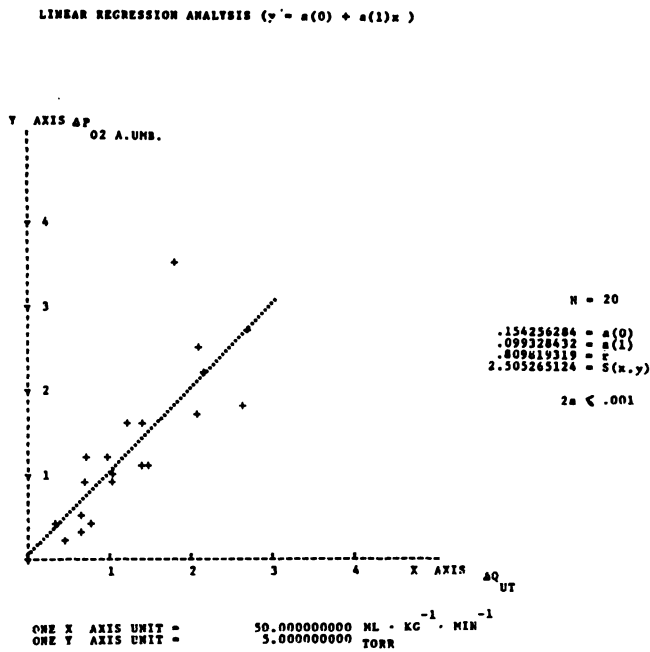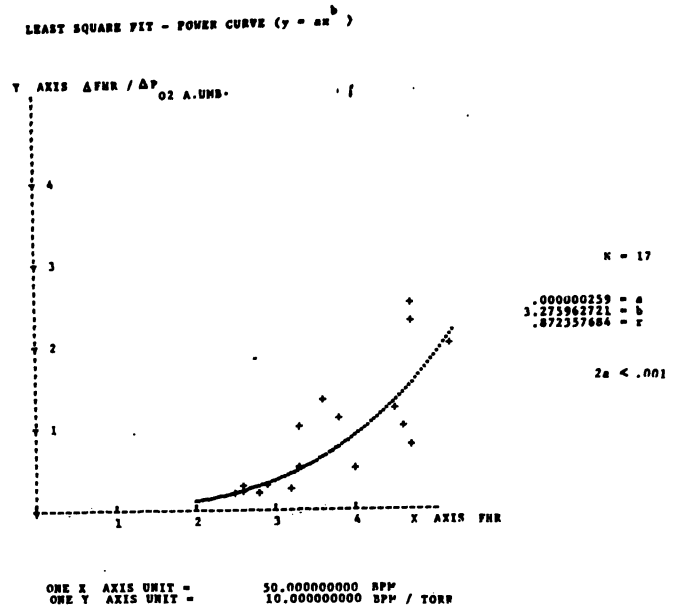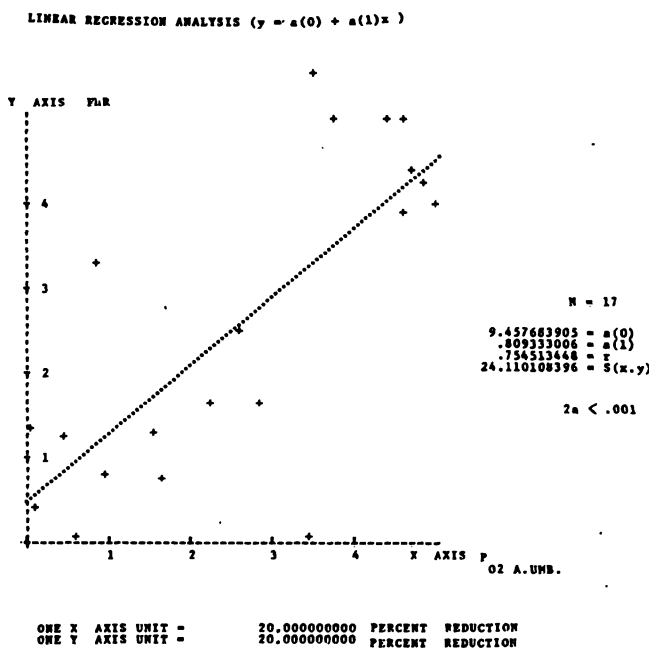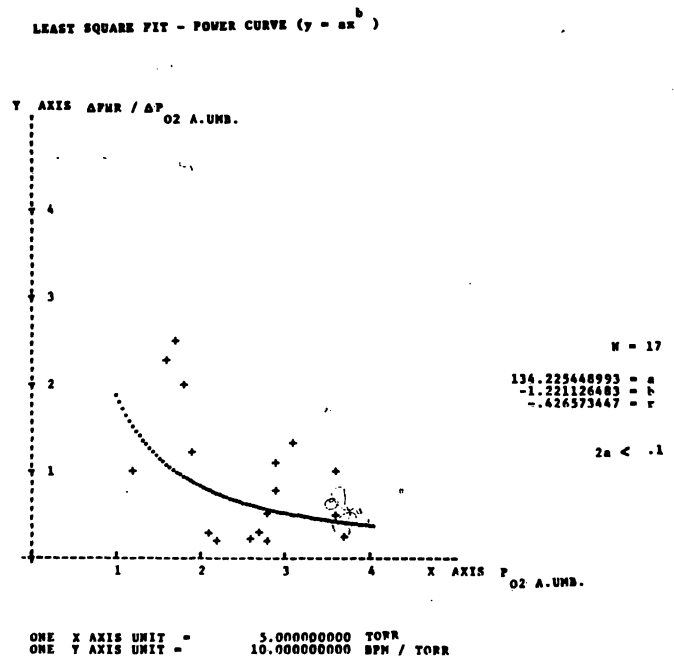
Fig. 13

Fig. 15

Fig. 14

Fig. 16

Fig. 13. Significant linear correlation between absolute values of ΔpO_2 in the umbilical artery and ΔQ_{UT} during moderate to severe hypoxemia. (Basal $pO_2 < 20$ Torr).

Fig. 14. Significant correlation between ΔFHR and ΔpO_2 in the umbilical artery, both taken as percentage of basal values. (See also legend to Fig. 8).

Fig. 15. Significant correlation between $\Delta FHR/\Delta pO_2$ ratio and basal FHR. Deceleration amplitude per unit of pO_2 decrease rises with rising basal FHR.

Fig. 16. Relationship between $\Delta FHR/\Delta pO_2$ ratio and basal pO_2. Correlation nearly significant. Deceleration amplitude per unit of pO_2 decrease rises with falling basal pO_2.
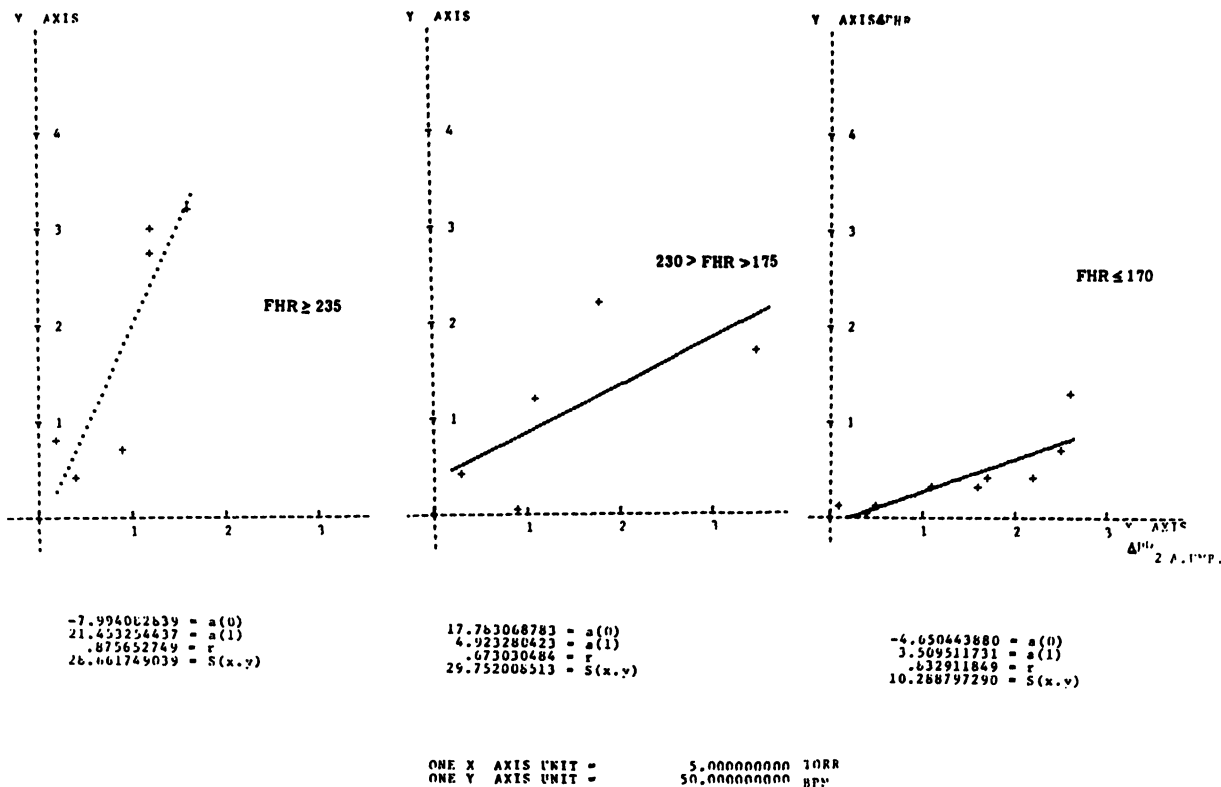
LINEAR REGRESSION ANALYSIS $(y = a(0) + a(1)x)$

Fig. 17. Relationship between absolute values of ΔFHR and ΔpO₂ for various levels of basal FHR. The slope of regression is rising with rising level of basal FHR.
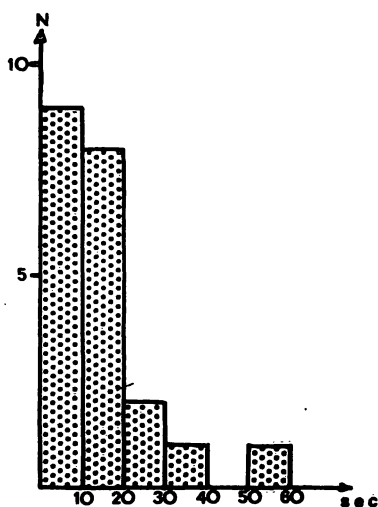
Fig. 18. Histogram of lag times between onset of UBF reduction and onset of FHR deceleration.

reduction. Ten min after the end of each reduction, but presumably much earlier mean pO₂ was in the initial range again. That means changes occur with a short time constant. Publications on continuous monitoring of pO₂ support this fact [14, 16, 24, 29, 30] though absolute data for the time constant are missing.

3.3 Mean pH decreased proportionally during reduction of UBF. In contrast to pO₂ 10 min after the end of the reduction phase the fetus had not recovered in respect to pH. In fact pH remained constantly lowered or even a slight further decrease could be seen. Our explanation for this phenomenon is the following:

Hypoxemia from UBF reduction leads to fetal cardiovascular reaction with redistribution of fetal

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circulation [4, 7, 10, 11, 12, 20, 25]. The initial rapid fall of pH during UBF reduction may be caused by hypercapnia and by an immediate lactat input from regions of fetal circulation with unchanged perfusion during hypoxemic fetal cardiovascular reaction. This component of lactat input has a short time constant and gives rise to the initial rapid pH fall. The secondary decrease of pH after cessation of UBF reduction may be the resultant of a delayed lactat input from regions of fetal circulation with diminished perfusion during hypoxemic redistribution, when these regions are reopened again on one side and overall lactat elimination on the other side.

Different time courses in the restitution from hypoxemia and acidosis after contraction elicited UBF reduction may explain well known findings taken from the dilatation phase of labors, for which a slight progressive fall of mean pH could be found despite a seemingly constant normal mean pO_2, especially when blood sampling is performed in the late phase of uterine relaxation. On the other hand, in the expulsion period a pO_2 fall along with a further fall of pH is seen [5, 13, 26, 34] despite of the short pO_2 time constant, because contractions become stronger and relaxation phase shortens.

3.4 Several items have to be discussed in regard to FHR changes. (It may be necessary to point out the fact again, that there was moderate to severe hypoxemia during the experimental sequences).

3.4.1 Mean FHR changes (Fig. 4) resembled the changes of UBF and pO_2, but 10 min after the end of the UBF reduction sequence mean basal FHR was slightly elevated and the explanation may be compensatory tachycardia.

3.4.2 The slopes of FHR descents and ascents varied. In general changes were more rapid when basal FHR was high and when UBF reduction was about 50% to 100%. On several occasions after UBF reduction of larger amount a secondary deceleration could be seen together with the secondary fall of UBF mentioned above (see Figs. 3 and Figs. 19). A biphasic deceleration like this by the way quite often can be seen in clinical FHR monitoring. The reason for this phenomenon is not quite clear. It might be a simultaneous rise in fetal blood pressure because injection of

epinephrine directly into the fetal buttock elicited a blood pressure rise and UBF decrease as well as FHR fall (Fig. 19, right column).

3.4.3 Evaluation of relations between UBF reduction and FHR decrease (Fig. 7) was disappointing at first glance. The key to understanding was the fact that there is an alinear correlation between relative values only when 100 bpm (the lowest heart rate seen with complete UBF reduction) is taken as $\emptyset$ %. And this correlation of relative values points to the fact that there is a dependency from basal UBF and FHR values. This dependency can be seen clearly in Figs. 9 and 10.

According to others and own results [17, 18, 22] the borderline to pathologic uterine blood flow near term seems to be in the range of about 100 ml/kg/min in various species. In fact, uterine O_2 uptake is reduced when UBf falls below 80—100 ml/kg/min. These findings are paralleled by our results in so far as the $\Delta FHR/\Delta Q_{UT}$ ratio is constantly low and independent of basal UBF and basal FHR as long as basal UBF is above this borderline and that this ratio increases sharply when UBF falls well below it. The same holds true for basal FHR but in the opposite direction because of the inverse relationship between basal UBF and basal FHR: there is a definite increase of the $\Delta FHR/\Delta Q_{UT}$ ratio when basal FHR is elevated to its maximum.

Figs. 11 and 12 give further information. Looking at the graphs for physiologic ranges of UBF and FHR (the graphs on the right sides) separately, it can be seen that in this range $\Delta FHR/\Delta Q_{UT}$ is a function of ΔQ_{UT} itself: UBF reduction up 50 ml/kg/min does not affect FHR at all. Only submaximal to complete reduction leads to minor decelerations. On the other hand, with falling UBF levels (and increasing FHR levels) the sole functional influence of ΔQ_{UT} is diminishing and the influence of basal UBF and basal FHR is getting into play (Figs. 11 and 12, graphs in the center and on the left).

3.4.4 Evaluation of our data verified a highly significant correlation between pO_2 decrease and UBF reduction for basal $pO_2 < 20$ Torr (Fig. 13). From this it is not surprising that the relationship between ΔFHR and ΔpO_2 to a large extent
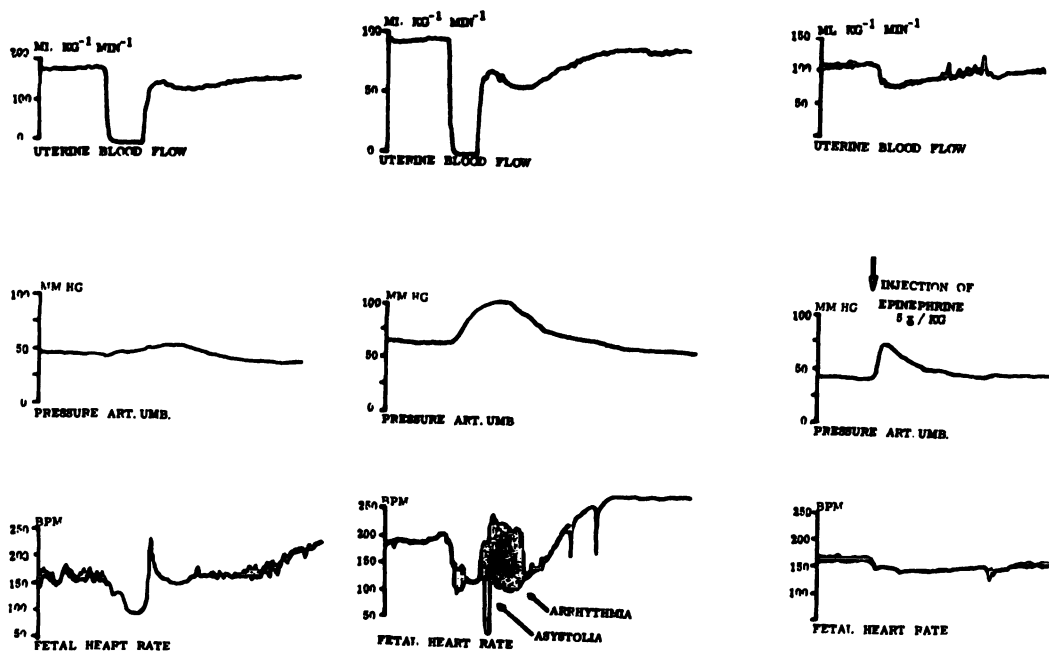
Fig. 19. Recordings of UBF (above), umbilical arterial pressure (middle) and FHR (below). Reaction of pressure and FHR on acute reduction of UBF.

A secondary fall of FHR and UBF after the end of acute UBF reduction can be seen simultaneusly with the rise in arterial pressure. (Graphs on the left and in the center). The latter may be the cause of secondary UBF and FHR reaction. Rise of arterial pressure after injection of epinephrine direct into the fetal buttock is accompanied by a fall in UBF and FHR. (Graph on the right).

resembles the relationship of ΔFHR and ΔQ_{UT}. Statistics though give poorer results (Figs. 14—17). This may be explained by the short time constant of pO_2 giving rise to more overall variation in pO_2 data. On the other hand one has to take in mind that progressive pH decrease caused a shift in the oxygen dissociation graph during the course of the experiment.

3.4.5 Our present data lead to the conclusion that no single parameter being analysed is responsible for FHR alterations solely. FHR response, i.e. deceleration amplitude is modified by basal values of UBF, fetal pO_2 and FHR and by the amount and slope of UBF reduction and consecutive pO_2 decrease. Thus the most extensive deceleration amplitudes were seen when all parameters were adversely altered. That the state of fetal oxygenation

and its acute changes have a major influence on the shape of FHR alterations has been shown by others [21, 27]. On the other hand one may argue that the level of basal FHR modifies deceleration amplitude too haging in mind WILDER's "Law of Initial Value" [31, 32], which in parallel has been adopted for defining heart rate regulation in the newborn [19, 28].

3.4.6 The lag time between the onset of UBF reduction and the onset of FHR deceleration turned out to be less than 11 sec in about 40% and less than 21 sec in 80% (Fig. 18). Although our results are taken from fetuses of ewes in general anaesthesia, they may hint to the fact that in severe hypoxemia the lag time may shorten. In fact a significant shortening of lag time with decrease of fetal arterial oxygen saturation and oxygen tension has been reported [21].

Summary

Five merino sheep near term were used for acute prepara-
tions to investigate the influence of basal uterine blood
flow (UBF), basal fetal oxygenation and basal fetal heart
rate (FHR) on FHR changes elicited by acute reduction
of UBF.
The ewes were anaesthesized with pentobarbital and
Alloferin was given for relaxation. Ventilation was main-
tained via a tracheal tube by a Starling pump. Maternal
heart rate, arterial pressure and intrauterine pressure as
well as fetal heart rate and umbilical artery pressure were
recorded continously. Initially blood flow was recorded
by cuff flow meter sequentially in both uterine arteries
for a short time in order to determine total UBF and the
ratio of flows. During the UBF reduction sequence flow
was recorded in the artery of the gravid horn continously
and measurement was corrected according to the initial
ratio of flows in both arteries, presuming that this ratio
would remain constant throughout the course of the
experiment.
Repetitive and progressive acute reduction of UBF
(approximately 25%, 50% and 100% from basal UBF
value) was achieved three times, lasting 120 sec each and
each approximatly 12 min apart, by flow meter controlled
partial or total occlusion of the aorta abdominalis of the
ewe with a balloon catheter inserted into the aorta. (In
some cases the lateral abdominal section was left open
and the aorta was compressed manually).
Before, 90 sec after the beginning and 10 min after the
end of UBF reduction blood samples were taken from the
fetal catheters (Fig. 3). In two preparations this sequence
was repeated once after complete recovery of FHR.

Results

Initial UBF values ranged from 180 to 57 ml/kg/min,
pO_2 in the umbilical artery was 18.5 to 6 Torr, pCO_2 was
37 to 57 Torr and pH 7.43 to 7.23 pH units. Basal FHR
ranged from 130 to 235 bpm. Thus wide ranges of UBF
as well as fetal cardiovascular and biochemical situations
were under investigation. Altogether low basal UBF was
accompanied by fetal hypoxemia and tachycardia. The
time courses of UBF, pO_2, pCO_2 and pH in the umbilical

artery and of FHR in connection with repetitive acute
reduction of aortic flow were the following:
UBF dropped rapidly on reducing aortic blood flow. On
release of the aortic obstruction it rose as rapidly again,
but on 50% to 100% reduction this rise was sometimes
followed by a slight rebound fall that gradually faded out.
Mean pO_2 in the umbilical artery, initially in the moderate
to severe hypoxemic level, fell rapidly and proportionally
to the amount of UBF reduction. Ten minutes after the
end of each reduction, but presumably much earlier mean
pO_2 was in the initial range again. Mean pH decreased
proportionally during reduction of UBF. In contrast to
pO_2 10 min after the end of the reduction phase the fetus
had not recovered in respect to pH. In fact, pH remained
lowered or even a slight further decrease could be seen.
Mean FHR changes resembled the changes of UBF and
pO_2, but 10 min after the whole UBF reduction sequence
mean basal FHR was slightly elevated.
As to the relationship between acute reduction of UBF
(ΔQ_{UT}) and FHR decrease (ΔFHR) an alinear correlation
between the values, expressed as percentage of basal level,
could be verified. This fact leads to the conclusion that
the $\Delta FHR/\Delta Q_{UT}$ ratio is dependent on basal values of
UBF and FHR: statistics reveal that within physiologic
levels of UBF and FHR minor and moderate acute UBF
reductions do not affect FHR at all or lead to minor
decelerations. Only substantial reductions will cause
decelerations of larger amplitude. But with decreasing
basal UBF levels (and increasing FHR levels) the same
absolute amount of UBF reduction leads to increasing
deceleration amplitudes.
As it is widely accepted that FHR decelerations caused by
acute UBF reduction are mediated by a fall in fetal pO_2,
the relations between acute UBF reduction and pO_2 fall
in the umbilical artery were investigated and a highly
significant linear correlation could be found. Therefore
the same relations between ΔFHR and ΔpO_2 should be
expected as between ΔFHR and ΔQ_{UT}. This holds true
in general but statistics give poorer results, probably
because the short time constant of pO_2 gives rise to more
overall variation in pO_2 data. On the other hand one has
to take in mind that progressive pH decrease caused a shift
in the oxygen dissociation graph during the course of the
experiment.
The lag time between onset of UBF reduction and onset
of FHR deceleration was less than 11 sec in about 40%
and less than 21 sec in 80%.

Zusammenfassung

Akute Verminderung der Uterusdurchblutung und Ver-
änderungen der fetalen Herzfrequenz beim Schaf am Ende
der Tragzeit.
Es sollte der Einfluß der basalen Uterusdurchblutung, der
basalen fetalen Oxygenation und der basalen fetalen
Herzfrequenz auf die durch akute Drosselung der Uterus-
durchblutung hervorgerufenen fetalen Herzfrequenzver-
änderungen untersucht werden. Dazu wurden 5 hoch-

trächtige Merinoschafe mit Pentobarbital narkotisiert
und mit Alloferin relaxiert. Die Ventilation wurde nach
Tracheotomie und Intubation mit einer Starling-Pumpe
aufrechterhalten. Die materne Herzfrequenz, der materne
arterielle Druck, der Intrauterindruck, die fetale Herz-
frequenz, der Druck in der Arteria umbilicalis wurden
kontinuierlich registriert. Vor der eigentlichen Versuchs-
durchführung wurde die Durchblutung mit einem Cuff-

flowmeter hintereinander kurzzeitig in beiden Uterin-
arterien gemessen und die Gesamtuterusdurchblutung
sowie das Verhältnis beider bestimmt. Während des
Drosselungsversuches wurde die Durchblutung auf der
Seite des graviden Horns kontinuierlich registriert und die
Eichskala entsprechend dem Durchblutungsverhältnis in
beiden Arterien auf die Gesamtdurchblutung korrigiert.
Eine wiederholte und jeweils zunehmende Drosselung der
Uterusdurchblutung (nährungsweise 25%, 50% und 100%
vom Ausgangswert der Durchblutung) von jeweils 120 sec
Dauer und etwa im Abstand von 12 min wurde durch
partielle oder totale Verlegung der Aorta abdominalis des
Muttertieres mit einem Ballonkatheter erreicht. (In einigen
Fällen blieb die Laparotomiewunde offen und die Aorta
wurde manuell komprimiert). Vor, 90 sec nach Beginn
und 10 min nach Ende der Durchblutungsdrosselung
wurden Blutproben zur Bestimmung von PO_2, PCO_2 und
pH aus dem in einem Ast der Arteria umbilicalis liegenden
Katheter entnommen. Bei 2 Schafen wurde die Drosse-
lungssequenz nach Stabilisierung der fetalen Herzfrequenz
wiederholt.

Ergebnisse

Die Ausgangswerte für die Uterusdurchblutung lagen
zwischen 180 und 57 ml/kg/min, der pO_2 in der Arteria
umbilicalis wurde mit 18,5 bis 6 Torr, der pCO_2 mit 37
bis 57 Torr und pH mit 7,43 bis 7,23 pH-Einheiten be-
stimmt. Das fetale basale Herzfrequenzniveau lag zwischen
130 und 235 Spm. Damit kamen also weite Bereiche basa-
ler Uterusdurchblutung und fetaler kardiovaskulärer und
biochemischer Situationen zur Auswertung. Insgesamt
fand sich bei erniedrigter Uterusausgangsdurchblutung
eine Tendenz zu fetaler Hypoxämie und Tachykardie.

Die Zeitgänge von Uterusdurchblutung, pO_2, pCO_2 und
pH in der Arteria umbilicalis sowie der fetalen Herzfrequenz
bei akuter und wiederholter Aortendurchblutungsdrosse-
lung waren folgende: es kam zum steilen Abfall der Uterus-
durchblutung. Nach Beendigung der Aortenkompression
stieg die Uterusdurchblutung ebenso steil wieder an. Bei
50 bis 100%iger Drosselung jedoch folgte diesem Wieder-
anstieg gelegentlich ein leichter Wiederabfall, der dann
langsam abklang. Der pO_2-Mittelwert in der Arteria umbili-
calis, schon vor der Drosselungssequenz im Bereich mittle-
rer bis schwerer Hypoxämie, fiel steil und proportional
zum Ausmaß der Uterusdurchblutungsdrosselung. 10 min
nach Ende jeder Drosselung, wahrscheinlich aber viel

früher, fand sich der pO_2-Mittelwert wieder im Ausgangs-
bereich. Der pH-Mittelwert fiel während der Drosselung
proportional ab. Im Gegensatz zum pO_2 hatte sich der
Fet 10 min nach Ende der Drosselung in Bezug auf den
pH-Wert aber noch nicht erholt: der pH-Wert blieb viel-
mehr erniedrigt, bzw. es wurde sogar ein weiterer pH-
Abfall beobachtet. Der Mittelwert der fetalen Herzfre-
quenz verhielt sich analog den Veränderungen der Uterus-
durchblutung und dem pO_2, allerdings fand sich 10 min
nach Ende der Drosselungssequenz eine leichte Frequenz-
erhöhung.
Es gelang der Nachweis einer alinearen Korrelation
zwischen den prozentualen Werten der akuten Uterus-
durchblutungsdrosselung und der Herzfrequenzdezele-
ration. Das deutet darauf hin, daß das Verhältnis $\Delta FHR/
\Delta Q_{UT}$ von den Ausgangswerten der Uterusdurchblutung
und der fetalen Herzfrequenz abhängig ist. Die weitere
statistische Aufarbeitung zeigt, daß im Bereich physiolo-
gischer Uterusdurchblutung und fetaler Herzfrequenz
leichte und mittlere Drosselungen der Uterusdurchblutung
die Herzfrequenz nicht beeinflussen, allenfalls minimale
Dezelerationen hervorrufen und nur erhebliche Durch-
blutungsdrosselungen zu Dezelerationen größerer Ampli-
tude führen. Mit sinkender Ausgangsuterusdurchblutung
(oder steigender fetaler Herzfrequenz) erzeugt die gleiche
absolute Durchblutungsdrosselung jedoch Dezelerationen
zunehmender Amplitude.
Weil angenommen wird, daß die durch Uterusdurch-
blutungsdrosselung bedingten Dezelerationen durch
einen pO_2-Abfall hervorgerufen werden, wurden auch
die Beziehungen zwischen der Uterusdurchblutungs-
drosselung und dem pO_2-Abfall in der Arteria umbilicalis
untersucht. Dabei fand sich ein hoch signifikant linearer
Zusammenhang. Deshalb sollten zwischen dem pO_2-Ab-
fall und der Dezelerationsamplitude die selben quantita-
tiven Beziehungen bestehen wie zwischen der Uterus-
durchblutungsdrosselung und der Dezelerationsamplitude.
Das ließ sich im vorliegenden Datenmaterial in der Tendenz
auch nachweisen, doch waren die statistischen Ergebnisse
nicht so eindeutig. Möglicherweise führt die kurze Zeit-
konstante des pO_2 zu mehr Variationen bei den pO_2-
Daten. Andererseits muß bedacht werden, daß der zu-
nehmende pH-Abfall während der Dauer des Experiments
eine Verschiebung der O_2-Dissoziations-Kurve erzeugte.

Die Verzögerungszeit zwischen dem Beginn der Uterus-
durchblutungsdrosselung und dem Beginn der Dezeleration
lag in etwa 40% unter 11 sec und in 80% unter 21 sec.

Schlüsselwörter: Azidose, CTG, Dezeleration, Durchblutung (uterim), Fet, Herzfrequenz (fetale), Hypoxämie, Tierver-
such, Verzögerungszeit.

Résumé

Jugulation de la circulation du sang dans l'uterus et alterations du rhythme cardiaque foetal chez les brebis enceintes approchant du terme
L'article présent traite de l'influence de la circulation
sanguine utérine de base, de l'oxygénation et de la
fréquence cardiaque basales du foetus sur les altérations
du rhythme cardiaque foetal résultant d'une jugulation

aigue de la circulation utérine. A cet effet, on a administré
à 5 brebis mérinos en stade avancé de grossesse une narcose
de pentobarbital et un relaxant d'alloférine. La ventilation
a été maintenue après trachéotomie et intubation avec
une pompe Starling. La fréquence cardiaque et la pression
artérielle de la mère, la pression intrautérine, la fréquence
cardiaque du foetus, la pression dans l'artère ombilicale

ont été enregistrées de façon continue. Avant de procéder à l'examen proprement dit, on a utilisé un Cuff-flow meter pour mesurer à brefs intervalles la circulation sanguine dans les deux artères utérines, ce qui a permis d'observer l'ensemble de la circulation utérine et le rapport entre la circulation des deux artères. Durant toute la séquence de jugulation on a enregistré de façon continue la circulation dans l'artère de la corne gravide et corrigé les mesures en accord avec le rapport initial entre la circulation des deux artères, ce rapport étant supposé constant tout au long de l'expérimentation. Une jugulation aigue de la circulation sanguine dans l'utérus, progressive et répétée trois fois (environ 25%, 50% et 100% de la valeur de base de la circulation utérine), d'une durée respective de 120 sec. et à intervalles approximatifs de 12 min', a été effectuée par occlusion partielle ou totale de l'aorte abdominale de la femelle mère à l'aide d'un cathéter à ballon. (Dans quelques cas, l'ouverture de la la parotomie a été maintenue béante pour permettre la compression manuelle de l'aorte). Avant la jugulation sanguine, 90 sec. après son début et 10 min. après sa fin, du sang a été prélevé dans le cathéter placé dans le cathéter placé dans une branche de l'artère ombilicale pour définir le pO_2, le pCO_2 et le pH. Chez 2 brebis, la séquence de jugulation a été répétée après stabilisation complète de la fréquence cardiaque du foetus.

Résultats:

Les valeurs initiales de la circulation sanguine utérine se sont situées entre 180 et 57 ml/kg/min; le pO_2 de l'artère ombilicale a varié entre 18,5 et 6 Torr, le pCO_2 entre 37 et 57 Torr et le pH entre 7,43 et 7,23 unités pH. Le niveau initial de fréquence cardiaque du foetus se situa entre 130 et 235 bpm (battement/min). C'est ainsi qu'on a pu évaluer également des problèmes assez vastes de la circulation sanguine utérine basale et des situations cardio-vasculaires et biochimiques chez le foetus. Dans l'ensemble. on observa une tendance à l'hypoxémie et tachycardie foetales dans les cas d'un niveau bas de circulation utérine initiale.

Les temps de circulation sanguine utérine, de pO_2, pCO_2 et pH dans l'artère ombilicale ainsi que de la fréquence cardiaque foetale en cas de jugulation aigue et répétée de la circulation aortique ont été les suivants: baisse rapide de la circulation utérine qui a remonté aussi rapidement une fois cessée la compression aortique. Mais dans les jugulations de 50 à 100%, cette remontée a été occasionnellement suivie d'une légère rechute qui s'atténua peu à peu. La moyenne du pO_2 dans l.artère ombilicale, qui se situait initialement au niveau d'hypoxémie modérée à grave, baissa brusquement et de façon proportionnelle à

l'importance de la jugulation de la circulation utérine. 10 min après chaque jugulation, mais probablement beaucoup plus tôt, la moyenne du pO_2 retrouvait à peu près son niveau de départ.

La moyenne du pH baissa de façon proportionnelle pendant la jugulation. En ce qui concerne le pH et au contraire du pO_2, le foetus n'agit pas encore récupéré 10 min après l'arrêt de la jugulation: en effet, la valeur du pH resta plutôt basse et subit même occasionnellement une nouvelle et légère chute. La moyenne de la fréquence cardiaque du foetus se comporta de façon analogue aux modifications de la circulation utérine et au pO_2; mais on observa une légère hausse de la fréquence initiale moyenne 10 min après la fin de la séquence de jugulation.

On a pu vérifier une corrélation alinéaire entre les valeurs exprimées en pourcentage du niveau initial relatives à la jugulation aigue de la circulation utérine (ΔQ_{UT}) et à la décélération de la fréquence cardiaque (ΔFHR). D'où on peut conclure que le rapport $\Delta FHR/\Delta Q_{UT}$ dépend des valeurs initiales de la circulation sanguine utérine et de la fréquence cardiaque du foetus: Les évaluations statistiques montrent qu'en ce qui concerne la circulazion utérine physiologique et la fréquence cardiaque foetale, les jugulations légères et moyennes de la circulation utérine n'influencent pas la fréquence cardiaque ou provoquent au plus des décélérations mineures et que seules les jugulations très fortes causent des décélérations importantes. Par contre, en cas de baisse de la circulation utérine initiale (et de hausse de la fréquence cardiaque foetale), la même jugulation absolue de la circulation produit des décélérations d'amplitude croissante.

Etant admis que les décélérations causées par la jugulation aigue de la circulation sanguine utérine sont provoquées par une chute du pO_2 foetal, on a examiné les rapports entre la jugulation de la circulation utérine et la chute du pO_2 dans l'artère ombilicale et observé une corrélation linéaire très significative. D'où on conclut qu'il doit exister entre la baisse du pO_2 et l'amplitude de décélération les mêmes rapports quantitatifs qu'entre la jugulation de la circulation utérine et l'amplitude de décélération. Si les données présentes parlent en ce sens, les résultats statistiques ne sont pas aussi clairs. Il est possible que la courte constante de temps du pO_2 soit à l'origine d'une plus grande fluctuation dans les données du pO_2. Par ailleurs, il faut considérer que la baisse progressive du pH pendant la durée de l'expérience a produit un déplacement de la courbe de dissociation de O_2.

Le temps de retard entre le début, d'une part, de la jugulation de la circulation sanguine utérine et, d'autre part, de la décélération de la fréquence cardiaque a été inférieur à 11 sec. dans 40% des cas et inférieur à 21 sec dans 80% des cas.

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Priv. Doz. Dr. Heinz-Dieter Junge
Department of Obstetrics and Gynecology
University of Würzburg
Josef-Schneider-Str. 4
D-8700 Würzburg