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Catecholamines in arterial and venous umbilical blood: placental extraction, correlation with fetal hypoxia, and transcutaneous partial oxygen tension

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1 Introduction

Investigations performed in animal experiments [6, 7, 16, 17, 19] as well as in man [2, 3, 9, 10, 18, 20, 25] suggest that fetal hypoxia is associated with an increase in circulating catecholamines due to sympathoadrenal stimulation. The correlation between catecholamines and cardiovascular, respiratory, and metabolic changes as determined during intrapartum fetal monitoring by means of cardiotocography (CTG), fetal blood gas analysis, and measurement of the transcutaneous partial oxygen tension ($tcpO_2$) has not yet been exhaustively investigated. The effect of fetal hypoxia on the dopamine concentration in cord blood likewise has not been explored.

These gaps in our knowledge are attributable to some extent to methodological factors. The older (fluorimetric) tests, which require blood volumes of 15–20 ml, are restricted to the detection of epinephrine (E) and norepinephrine (NE) in mixed cord blood [3, 22] or venous umbilical blood [18, 23], and some studies only measured total catecholamines [2, 20] without further differentiation. In contrast, the radioenzymatic single-isotope technique [8, 29] allows the specific measurement of E, NE and the third catecholamine, dopamine (D), in 0.1–0.2 ml plasma. With the advent of this method it has become possible to reassess the following questions of clinical interest:

1. To what extent are free catecholamines, varying over a wide range from normal to exceptionally high values, extracted across the human placenta?
   What interrelationship exists between the extraction rates of NE, E, and D?
2. How are fetal hypoxia, acidosis, changes in fetal heart rate (FHR), and postpartum fetal distress associated with the catecholamine levels in fetal plasma?
3. Is an increased secretion of catecholamines in the human fetus accompanied by a fall in $tcpO_2$, as has previously been suggested though only on the basis of animal experiments [16, 19, 28]?

Curriculum vitae

RENE PAULICK, *M. D., was born in January, 1956 in Hannover, Germany. Medical studies in Würzburg from 1974 to 1980. He is at present assistent at the Department of Obstetrics and Gynecology, University of Würzburg (Head: Prof. Dr.* K.-H. WULF). *Chief area of interest: Fetal and neonatal physiology, gynecological oncology.*

2 Methods

The patients in our study comprised 34 parturient women aged 19–34 years who after essentially

uncomplicated pregnancies (duration of pregnancy 36–41 weeks) were delivered vaginally (30 spontaneous births, 4 vacuum extractions). The birth weights ranged from 2450–4460 g. Free catecholamine concentrations were determined separately in arterial and venous umbilical blood following immediate clamping of the cord, and in samples of maternal blood obtained immediately after delivery from the brachial vein.

After collection the blood was at once transferred into chilled polypropylene tubes to which had been added, as anticoagulant and antioxidant, 50 µl of a solution containing 76 mg/ml EGTA (ethyleneglycol-bis-(β-aminoethyl ether) N,N,N'-tetraacetic acid) and 48 mg/ml reduced glutathione. In some of the later experiments, lithium-heparin tubes (SARSTEDT No. 36 377) were used since comparative studies had shown that catecholamine concentrations can be measured with equal accuracy in heparinized plasma and antioxidant-containing heparinized plasma, but not in EDTA-containing plasma. It is important however that tubes are placed on ice without delay [36]. Hemolyzed samples were discarded. After centrifugation for 10 minutes (4000 rpm) at + 2 to + 4 °C, the plasma was kept frozen at − 25 °C until assayed.

The concentrations of free NE, E, and D were assayed radioenzymatically using a modified and shortened version of the method of PEULER and JOHNSON [8, 29, 36]. The sensitivity of the method is below 1 pg/ml for NE, E, and D, with intra-assay and inter-assay coefficients of variation of approx. 3 % and 10 %, respectively.

The acid-base balance and blood gases were assessed with the TECHNICON Gas Analyzer. The base deficit in the extracellular fluid was calculated nomographically by the method of SIGGAARD-ANDERSEN from the pH and pCO_2 in the umbilical artery, hemoglobin concentration 5 g% [33].

For interpretation of the cardiotocograph (CTG) tracings, the deceleration areas obtained during the last hour antepartum were measured planimetrically in cm^2/h (chart speed: 1 cm/min; FHR amplitude: 1 cm = 20 bpm). The baseline heart rate was determined every 2 minutes, followed by calculation of mean values.

In 22 parturient women the fetal $tcpO_2$ was continuously monitored with an oxygen electrode (TRANSOXODE/Hellige) during the late first stage and the second stage of labor. At the same time, the catecholamine concentrations in the umbilical vessels were measured in 14 patients. The electrode was applied to the fetal scalp by means of a self-adhesive tissue glue (HISTO-ACRYL, Braun Melsungen). The temperature of the electrode was adjusted to 44 °C. After attainment of a stable level, the $tcpO_2$ was recorded for 92 ± 71 (SD) minutes on average. The mean $tcpO_2$ values determined at 10-minute intervals were used to calculate during the last hour before delivery the overall means. By simultaneously recording the relative local skin perfusion, distinct artefacts could be identified and excluded [14].

The statistical analysis and significance calculations were performed at the Computer Center of Würzburg University (Dr. I. HAUBITZ). The correlation coefficients were calculated using either the Spearman rank correlation test (when there was no normal distribution) or the Kendall rank correlation test (when 'ties' were present).

3 Results

3.1 Catecholamine concentrations in arterial and venous cord blood; placental catecholamine extraction: The free catecholamine levels measured in arterial and venous cord blood may vary substantially (Fig. 1). The mean NE concentration was 10,200 pg/ml (range 1,500–74,100 pg/ml) in arterial cord blood and 2,650 pg/ml (range 200–30,700 pg/ml) in venous cord blood. The concentrations of E in arterial and venous cord blood were 1,120 pg/ml (range 140–4,030 pg/ml) and 280 pg/ml (range 25–1,790 pg/ml), respectively.

The concentrations of circulating free D approximated 130 pg/ml (range 30–660 pg/ml) in arterial cord blood, and 70 pg/ml (range 15–320 pg/ml) in venous cord blood.

The placental catecholamine extraction rate (ER), calculated from the concentrations in the umbilical

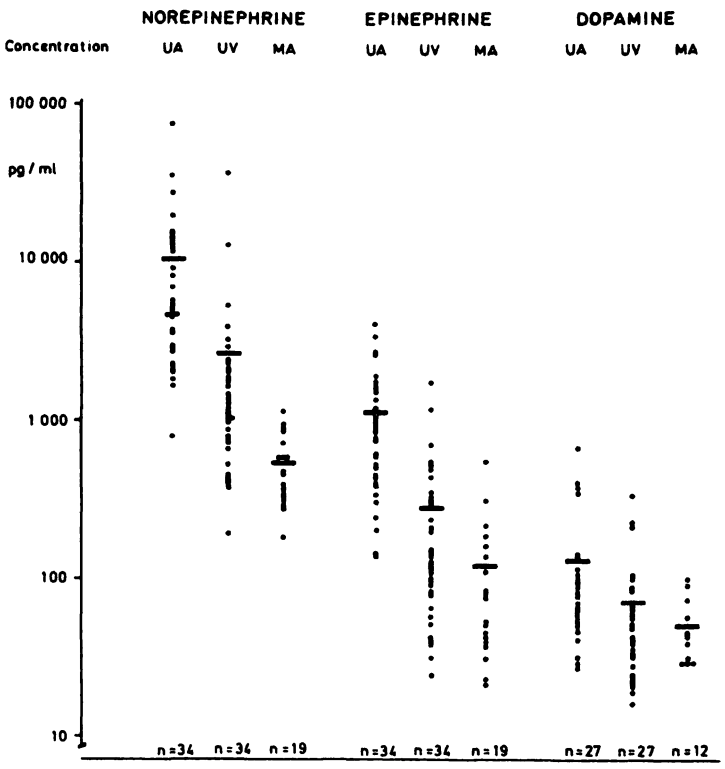

Fig. 1. Concentrations of free NE, E and D in the umbilical artery (UA), umbilical vein (UV) and in maternal venous (brachial vein) blood (MA) at the time of delivery.

artery (C_{ua}) and umbilical vein (C_{uv}) according to the formula

$$ER = \frac{C_{ua} - C_{uv}}{C_{ua}} \cdot 100$$

was established as 77 ± 14% (range 41–96) for NE, 76 ± 16% (range 33–96) for E, and 33 ± 25% (range 24–99) for D.

There was a significant correlation between the extraction rates of E and NE (Fig. 2).

The umbilical arteriovenous difference in NE and E concentration rose in proportion to the arterial catecholamine concentration (Fig. 3).

3.2 Catecholamine concentrations in maternal blood: At the time of delivery, the mean free NE concentrations in the maternal venous blood were 540 pg/ml (range 180–1,120 pg/ml) (Fig. 1). In the majority of the patients, the NE levels thus exceeded the normal range of 100–450 pg/ml that had been determined using the same method in normotensive male and female subjects under conditions of rest [36].

The concentrations of free E in the maternal blood, 120 pg/ml (range 20–550 pg/ml), were likewise

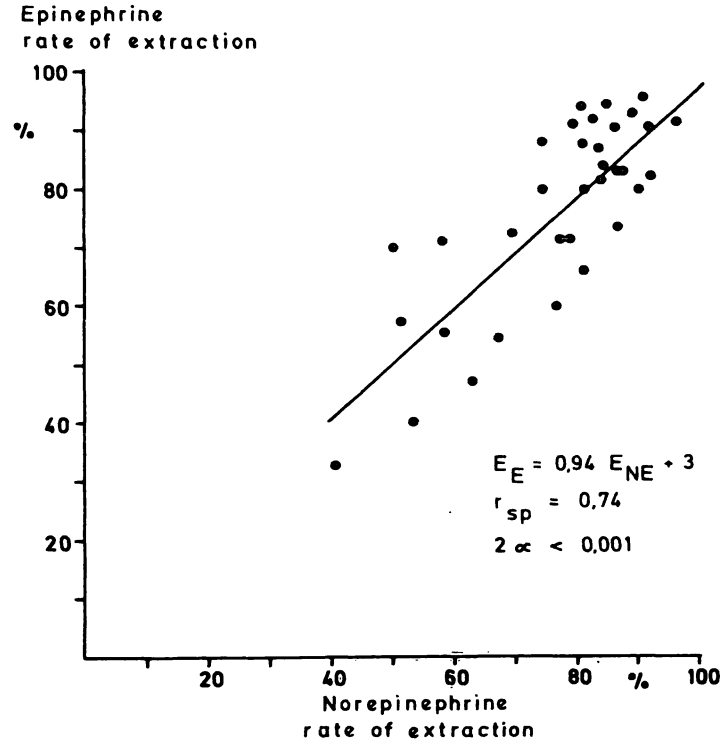

Fig. 2. Correlation between the extraction rates of E (ER_E) and NE (ER_{NE}) during placental passage. Extraction rates vary between 35 % and 95 %. A highly significant correlation is demonstrated. There is no difference between the regression line and the line of identity.

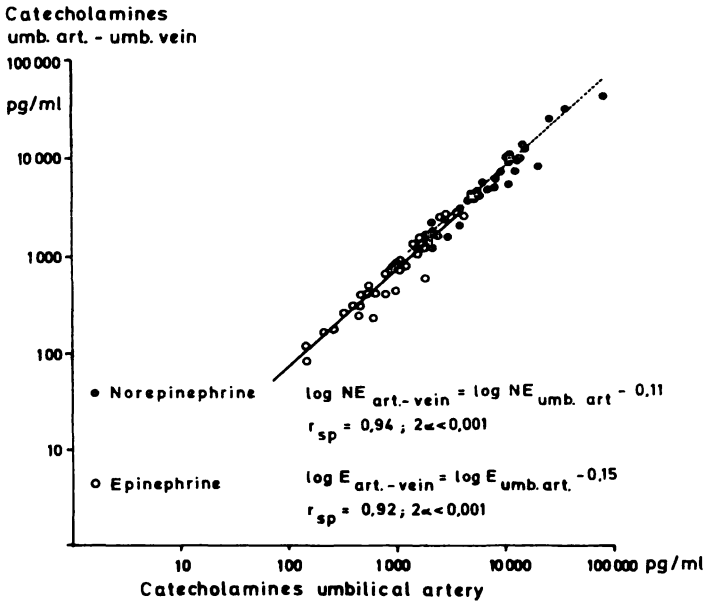

Fig. 3. Correlation between the arterio-venous concentration difference of E and NE and arterial concentrations. A linear relationship is demonstrated in the range below 4.000 pg/ml for E and 74.000 pg/ml for NE, suggesting that the placental catecholamine extraction does not reach full saturation.

increased over the normal E levels (20–95 pg/ml). In contrast, the mean concentrations recorded for free D, 50 pg/ml (range 30–100 pg/ml), were fairly unchanged compared to the normal range of 10–70 pg/ml.

2.3 Catecholamines and fetal hypoxia: As shown in Figs. 4 and 5, there was a highly significant relationship between the umbilical arterial NE levels, neonatal status (as assessed by the 1-minute APGAR score), and metabolic acidosis (determined by pH and base deficit). In some cases, the NE concentrations in the fetal blood were exceedingly high when associated with low Apgar scores and increasing metabolic acidosis. Analysis of the FHR in the last hour preceding delivery also revealed a significant relation between the area of deceleration, the baseline FHR, and the umbilical arterial NE concentrations. The fetal NE concentrations were found to rise as the deceleration area and baseline FHR increased (Fig. 6).

Fig. 7 gives a more detailed description of the correlation that exists between deceleration area, fetal tachycardia, and arterial NE concentration. It is seen that an increase of the deceleration area (> 15 cm^2/h) is not associated with elevated NE levels. A significant rise in the fetal arterial NE concentrations only occurs when tachycardia (> 150 b/min) supervenes.

Fetal arterial E concentrations as an indicator of enhanced release of the hormone from the adrenal medulla in conditions of stress, also demonstrate good correlations with the fetal parameters, although the correlation coefficients were lower than for NE (Figs. 4–6).

Unlike NE and E concentrations, the D levels in the umbilical vessels were affected by fetal hypoxia to a minor degree, only.

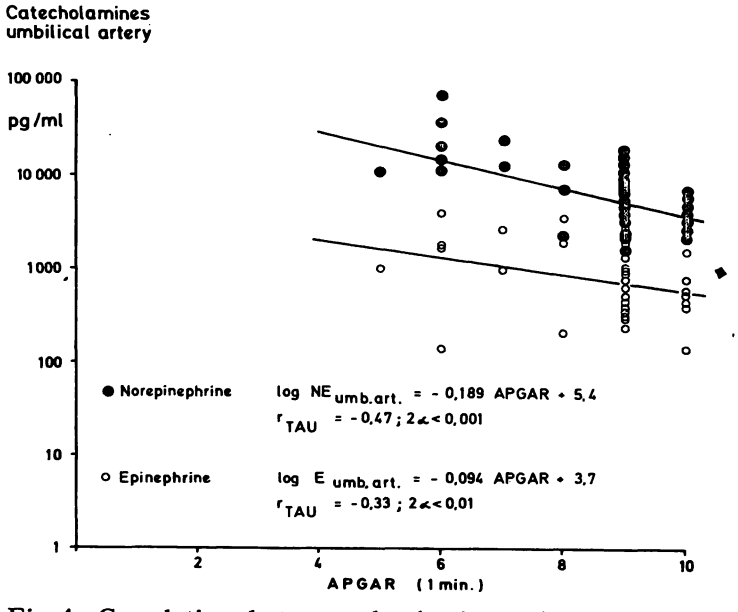

Fig. 4. Correlation between the 1-minute APGAR score and NE and E concentrations in the umbilical artery. Low APGAR scores are associated with increased catecholamine concentrations.

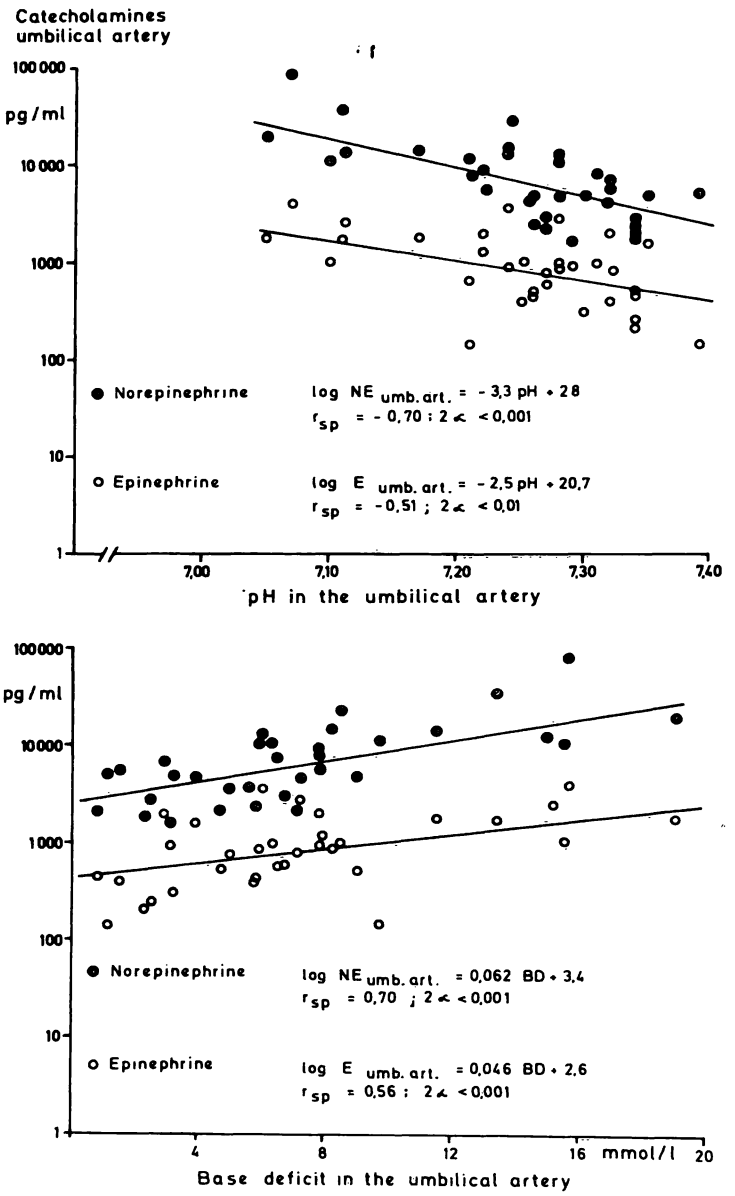

Fig. 5. Correlation between fetal arterial NE and E concentrations and metabolic acidosis measured by the pH and base deficit in the umbilical artery. Catecholamine concentrations start to rise with increasing metabolic acidosis.

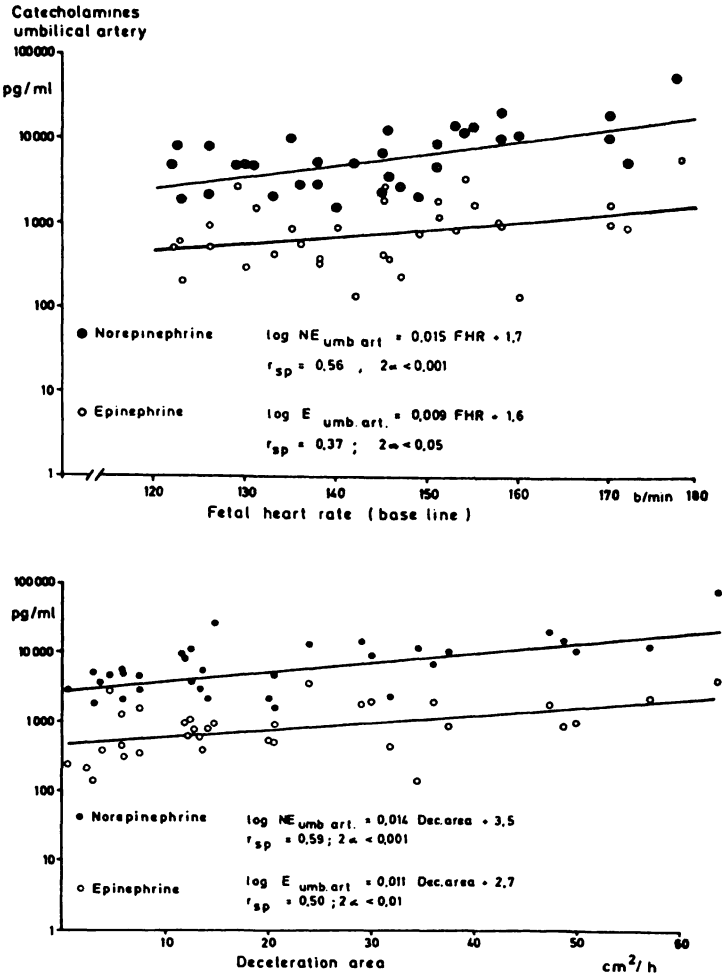

Fig. 6. Correlation between fetal arterial NE and E concentrations and baseline FHR and deceleration area during the last hour antepartum. Catecholamine concentrations rise with increasing deceleration area and baseline FHR.

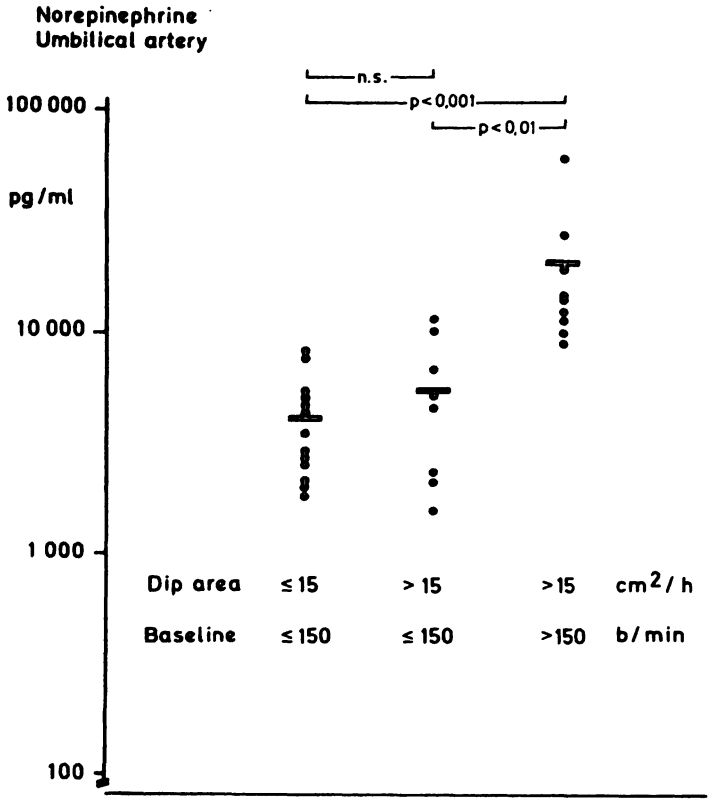

Fig. 7. Correlation between NE concentrations in the umbilical artery and alterations of the FHR. Alterations of the FHR are subdivided into deceleration area (≤ or > 15 cm^2/h) and baseline (≤ or > 150 b/min). An increase of the deceleration area without tachycardia is not associated with a rise of NE levels. Only with additional tachycardia, which often coincides with a loss of oscillation amplitude, a significant increase of fetal arterial NE levels can be observed.

3.4 Catecholamines, transcutaneous pO_2, and transcutaneous-arterial pO_2 difference: Fig. 8 illustrates the $tcpO_2$ values recorded during the 2 hours preceding parturition. They differ widely, ranging between 0–25 mm Hg and showing a tendency to decrease before delivery.

In Fig. 9, the mean $tcpO_2$ measured during the last hour before delivery is plotted against the NE concentration in the umbilical artery. There was a significant inverse relation with NE concentrations rising as $tcpO_2$ values decreased. No correlation could be detected between arterial E levels and the $tcpO_2$.

In most of the cases (70%), the $tcpO_2$ measured during the last hour before delivery was lower than the umbilical artery pO_2. This transcutaneous-arterial pO_2 difference (tc-art pO_2-d) was dependent on the NE concentration in the fetal arterial blood (Fig. 10) and was found to increase with rising NE concentration.

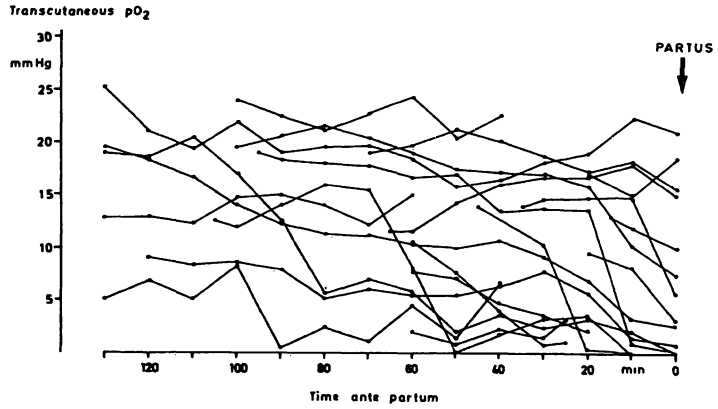

Fig. 8. Course of $tcpO_2$ during the last two hours before delivery. $tcpO_2$ values vary between 0 and 25 mmHg. In some cases a high $tcpO_2$ is recorded until delivery, while a fall in $tcpO_2$ can be demonstrated in other cases.

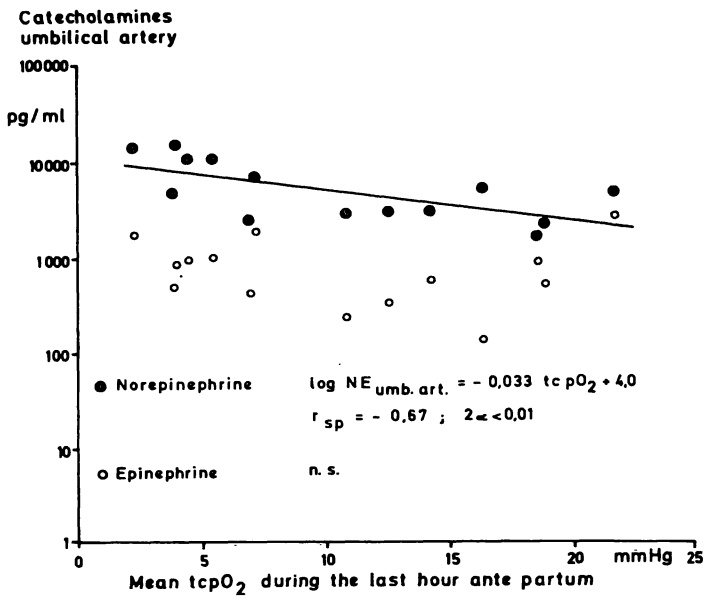

Fig. 9. Correlation between $tcpO_2$ in the last hour before delivery and NE and E concentrations in the umbilical artery. There is a significant inverse relationship: $tcpO_2$ decreases with increasing NE.

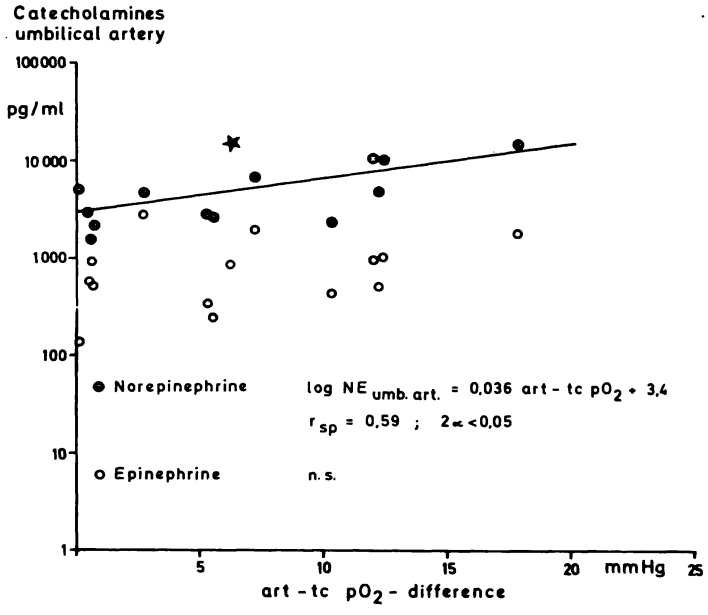

Fig. 10. Correlation between tc-art pO_2-d in the last hour before delivery and NE and E concentrations in the umbilical artery. With rising NE-secretion the tc-art pO_2-d increases. The correlation coefficient improved considerably after eliminating the value marked with an asterisk ($r_{sp} = 0.74$, $p < 0.01$). This was the only patient exhibiting low umbilical artery pO_2 (10.1 mmHg) at low oxygen saturation (< 20 %).

4 Discussion

4.1 Catecholamine extraction by the placenta: The fetal artery NE and E concentrations were in part excessively high, mean values being four times higher than in the umbilical vein and exceeding those in the maternal venous blood 20-fold for NE, and 10-fold for E (Fig. 1). These findings suggest that the catecholamines measured in cord blood are of fetal origin and that the placenta has a high capacity for inactivation of free catecholamines. At concentrations below 4000 pg/ml for E and 74,000 pg/ml for NE, a saturation of the placental catecholamine extraction was not detectable (Fig. 3).

It appears that the high placental catecholamine clearance is primarily attributable to metabolization of biogenic amines. Studies with radioactively labelled tracers have shown that the placental transfer accounts for only 5–10 % of the umbilical arteriovenous concentration difference [24, 31]. The enzymes catechol o-methyltransferase and monoamine oxidase, which are required for degradation of circulating catecholamines, have been demonstrated in placental tissue in high concentrations [5]. It also is probable that the biologic catecholamine inactivation is additionally effected by sulfate conjugation. Phenolsulfotransferase (EC 2.8.2.1), which is necessary for the conversion of free catecholamines to sulfated derivates has been isolated from human placental tissue [32].

Whereas umbilical artery E and NE concentrations were widely different, the extraction rates from the placenta with mean values of 75 % were found to be identical (Fig. 2). This was to be anticipated since the metabolic pathways of NE and E are identical. However, a comparison of the placental NE and E extraction with that of other organs revealed that the placental tissue occupies a unique position: on passage of catecholamines through the liver, cardiac and skeletal muscle, the NE extraction rate is invariably lower than that of E [4, 13]. The NE concentrations in the renal vein but also in the coronary sinus may even substantially exceed those measured in the arterial (afferent) blood [21, 26]. These observations suggest that in tissues with abundant sympathetic innervation NE is not only extracted but may also be released from postganglionic sympathetic nerve endings [21, 26]. As

a circulating hormone, E in contrast is released only from the adrenal medulla (and some brain areas) and extracted on its passage through the other organs. Hence, the different extraction rates of NE and E may be taken to reflect the density of sympathetic innervation and the sympathetic activity of an organ other than the adrenal medulla [4, 13, 21, 26]. In agreement with morphologic studies [30], the nearly identical placental extraction rates of NE and E indicate that sympathetic innervation is absent on the fetal side of the placenta.

4.2 Catecholamines and fetal hypoxia: Animal studies [6, 7, 16, 17, 19] and clinical investigations [2, 3, 10, 18, 20, 25] suggest that fetal hypoxic shock is associated with vigorous sympathoadrenal stimulation, as reflected by an increase in circulating catecholamines, especially in NE. This concept receives further support from the results reported in the present paper. The finding that stimulation of NE secretion is frequently accompanied by fetal hypoxia is in accord with the observations of KANEOKA et al. [18] and LAGERCRANTZ et al. [20]. The rise of the arterial E concentration is distinctly less pronounced and less constant. The average arterial concentration of free D is increased only 2.5-fold over maternal blood levels. It thus becomes obvious that D hardly responds to sympathoadrenal system stimulation.

Both pathologic alterations in FHR (decelerations, tachycardia) and hypoxic acidosis/postpartum depression are associated with increased arterial NE concentration. Various investigators have reported that analogous correlations exist between catecholamines, acid-base balance [2, 10, 18, 20], and the APGAR score [18, 25]. The results on FHR alterations and catecholamines are in part conflicting [2, 18, 20]. Unlike BISTOLETTI et al. [2], but in agreement with KANEOKA et al. [18], the present study evidences a quantitative relationship between the deceleration area and the arterial catecholamine levels (Fig. 6). More differentiated analysis of the deceleration areas reveals that an increase of the deceleration area exceeding 15 cm^2/h taken by itself is not associated with a rise in arterial NE (Fig. 7). It is only when an enlarged deceleration area coincides with fetal tachycardia that the NE concentration will increase substantially.

The findings in this study provide a differentiated confirmation of the relationship which exists, according to LAGERCRANTZ et al. [20], between a tachycardic baseline FHR and total catecholamines in the umbilical artery: Our observation that an increased baseline FHR is accompanied by a rise of both NE and E concentrations (Fig. 6) supports the concept that the development of tachycardia may reflect a circulatory compensation for acute changes in the blood oxygen content, as manifested by the hypoxic shock syndrome.

The above results suggest that decelerations signalling acute changes in fetal arterial pO_2 [19] cannot be taken to indicate the presence of a hypoxic shock syndrome with increased catecholamines merely on the strength of a quantitative analysis of the frequency, depth and duration of decelerations. Based on the available results, tachycardia should be evaluated as a supplementary parameter in the detection of fetal hypoxic shock.

There is no way of assessing to which extent other CTG features (e.g. loss of oscillation amplitude) can be employed as an indication of severe fetal hypoxia due to the heterogeneity of the CTG changes and the small number of tracings showing loss of oscillation **without** tachycardia.

4.3 Catecholamines, transcutaneous pO_2, and transcutaneous-arterial pO_2 difference: The results obtained on measurement of the $tcpO_2$ as described by HUCH [14] for intrapartum fetal monitoring are contradictory. Some authors reported good agreement between fetal arterial and transcutaneous pO_2 levels [11]. However, when pathological CTG alterations occur, $tcpO_2$ values are frequently lower than the pO_2 determined in arterialized fetal scalp blood [1, 15, 35]. In our studies, the $tcpO_2$ recorded during the two hours prior to delivery, varied between 0 and 25 mm Hg (Fig. 8). In the majority of cases, the $tcpO_2$ was lower than the arterial pO_2. Decreased $tcpO_2$ levels with development of a transcutaneous-arterial pO_2 difference (tc-art pO_2-d) were primarily seen with pathologic CTG changes.

What then is the explanation for this tc-art pO_2-d? Besides the epidermal thickness and possible measuring artifacts (e.g. pressure exerted on the electrode), the cutaneous blood flow is a major factor determining the results of $tcpO_2$ measurements. The $tcpO_2$ only corresponds to the arterial pO_2 when maximal vasodilatation, by warming the skin under the electrode to 42–43 °C with the heating element of the electrode, is achieved [12, 14, 27, 34]. Animal experiments have shown that the $tcpO_2$ varies from the arterial pO_2 after recurrent hypoxic episodes. It appears that vasoconstriction of cutaneous vessels due to increased release of NE during hypoxia may be responsible for the observed tc-art pO_2-d [6, 7, 16, 17]. The heating element of the electrode obviously is not always capable of maintaining optimal cutaneous blood flow. This assumption receives further support from the fall in $tcpO_2$ observed after injection of NE into experimental animals, the pO_2 in the arterial blood however remaining uneffected [19, 28].

In the present study, proof was furnished that in the human fetus hypoxic release of NE is closely correlated with the $tcpO_2$ in that NE levels rise with decreasing $tcpO_2$ (Figs. 9, 10). Stimulation of the sympathoadrenal system in hypoxic episodes causes peripheral vasoconstriction with pallor as it occurs in severely depressed neonates (so-called "pale asphyxia").

From a theoretical point of view, the relationship between NE and the tc-art pO_2-d should actually be nonlinear. The tc-art pO_2-d, which is low when NE levels are low, shows an initial increase with rising NE; with the appearance of severe hypoxia and a further increase in NE, the arterial pO_2 likewise starts to decrease. In the presence of severe hypoxia and a low arterial pO_2, the tc-art pO_2-d should consequently decrease again. This situation is depicted in Fig. 10 which shows considerable improvement of the correlation coefficient after elimination of one measuring point with an oxygen saturation below 20%.

The established correlation between fetal arterial NE levels and the fall in $tcpO_2$ lends additional support to the concept of KÜNZEL and JENSEN who had pointed to the potential of $tcpO_2$ monitoring in the diagnosis of a fetal hypoxic shock syndrome. These authors had shown that an increase in tc-art pO_2-d, together with the time interval during which a low $tcpO_2$ (0–3 mm Hg, the so-called "zero time") is recorded, are useful diagnostic tools in the detection of fetal shock [15]. On the other hand, it should be born in mind that even in the presence of a greatly reduced $tcpO_2$ the central artery pO_2, and hence the oxygen supply to vital organs unaffected by peripheral constriction (brain, heart, adrenal medulla), may not show a corresponding significant decrease. Also, there is a lack of exhaustive information as to which extent artifacts may affect the accuracy of transcutaneous monitoring (e.g. reduction in skin perfusion due to caput succedaneum or pressure exerted by the birth canal on the electrode).

5 Clinical consequences to be considered in the diagnosis of fetal hypoxic shock syndrome at time of delivery

For the obstetrician, the early detection of protracted fetal hypoxia as manifested by increased NE secretion, circulatory centralization, severe tissue hypoxia, and acidosis is of critical importance. While the diagnosis of acute fetal hypoxia presenting as continuous deceleration does not cause difficulty, the detection of hypoxic shock presenting as contraction-dependent decelerations poses a greater problem.

Based on the established interrelationship between increased catecholamine (NE) secretion and the various diagnostic parameters employed in intrapartum monitoring of the fetus, the diagnosis of hypoxic fetal shock syndrome is warranted if the following patterns are observed:

- wide and deep decelerations with an increased dip area and concurrent tachydardia
- severe metabolic acidosis of the fetus
- a greatly depressed $tcpO_2$ that has fallen to a few mm Hg (excepting artifacts)

The described investigations do not provide an answer as to how long fetal intrapartum hypoxia can be allowed to persist without creating a risk of late sequelae. Infants showing signs of extreme acidosis with concurrent release of catecholamines should therefore have a thorough follow-up.

Summary

In 34 parturient women the levels of free epinephrine (E), norepinephrine (NE), and dopamine (D) were determined by a radioenzymatic method using maternal venous and umbilical arterial and venous blood. The study was conducted to investigate the relationship between fetal catecholamines and hypoxia, fetal heart rate (FHR), and transcutaneous pO_2 ($tcpO_2$). The placental catecholamine extraction rates were also calculated.

Results

1. **The NE concentrations (10,200 pg/ml) and the E concentrations (1,120 pg/ml) in the fetal arterial blood were highly elevated with mean values increased 4-fold over umbilical vein values. Compared with the maternal venous blood, NE values were increased 20-fold, and E values 10-fold** (Fig. 1). Free D concentrations in fetal arterial blood (130 pg/ml) had risen 2.5-fold over maternal levels.
   These results suggest that the catecholamines measured in cord blood are of fetal origin and that the placenta has a high capacity for inactivation of free catecholamines. The placental extraction rate is 77 ± 14% for NE, 76 ± 16% for E, and 33 ± 25% for D (Fig. 2). The placental extraction rates for E and NE were virtually identical; in agreement with morphological studies they demonstrated absence of sympathetic innervation on the fetal side of the placenta.
2. **Highly significant correlations were found between fetal arterial NE concentrations and the 1-minute APGAR score, pH and base deficit in the umbilical artery and alterations of the FHR (deceleration area, baseline FHR)** (Figs. 4–6). Further analysis of FHR alterations (Fig. 7) reveals that an increase in deceleration area without tachycardia is not correlated with an increase of fetal arterial NE concentration. **A significant rise in NE was only found with additional tachycardia which is often associated with a loss of oscillation aplitude.**
   Fetal arterial E concentrations were found to correlate with the fetal parameters indicating increased adrenal secretion of the hormone during fetal stress. However, correlation coefficients were lower than those obtained for NE (Figs. 4–6). A significant effect of fetal hypoxia on arterial and venous D levels could not be demonstrated.
3. Fetal $tcpO_2$ varies between 0–25 mm Hg during the last two hours before delivery (Fig. 8). In most cases $tcpO_2$ was lower than the arterial pO_2. Besides epidermal thickness and artifacts, skin perfusion is a major factor influencing the $tcpO_2$ (transcutaneous arterial pO_2 difference). **Vasoconstriction of the cutaneous vessels induced by increased NE secretion during hypoxia may obviously produce a fall in $tcpO_2$.** This hypothesis receives support from the demonstration that the $tcpO_2$ is correlated with the fetal arterial NE concentration: $tcpO_2$ falls with rising NE and the tc-art pO_2-d increases (Figs. 9–10). The stimulation of the sympathoadrenal system during hypoxia results in peripheral vasoconstriction as manifested by the pallor of depressed neonates ("white asphyxia").

Clinical consequences

In view of the demonstrated correlation between increased catecholamine (NE) secretion and the various parameters for monitoring fetal intrapartum conditions, fetal hypoxic shock can be taken to be present if

- wide and deep decelerations with an increased dip area occur in combination with tachycardia,
- severe fetal metabolic acidosis is present,
- $tcpO_2$ is lowered to a few mm Hg (excluding artifacts).

Keywords: Cardiovascular system, catecholamines, dopamine, epinephrine, extraction rate, fetal heart rate, fetal shock, norepinephrine, transcutaneous pO_2, transcutaneous-arterial pO_2 difference.

Zusammenfassung

Katecholamine im arteriellen und venösen Nabelschnurblut: plazentare Extraktion, Beziehungen zur fetalen Hypoxie und zum transkutanen Sauerstoffpartialdruck
Bei 34 Gebärenden wurden im matern-venösen sowie arteriellen und venösen Nabelschnurblut die freie Adrenalin-(E), Noradrenalin-(NE) und Dopaminkonzentration (D) radioenzymatisch im Plasma bestimmt, um den Zusammenhang zwischen fetaler Katecholaminkonzentration, Hypoxie, fetalen Herzfrequenzveränderungen und transkutanen pO_2 zu untersuchen und die plazentare Katecholaminextraktion zu bestimmen.

Ergebnisse

1. **Im fetal arteriellen Blut finden sich zum Teil exzessiv erhöhte NE-(10 200 pg/ml)- und E-Konzentrationen (1120 pg/ml), die im Mittel 4fach höher als in der V. umbilicalis und beim NE 20fach und beim E 10fach höher liegen als im mütterlichen venösen Blut** (Abb. 1). Das zirkulierende freie D (130 pg/ml) ist im fetalarteriellen Blut um das 2,5fache gegenüber dem mütterlich venösen erhöht. Diese Befunde sprechen dafür, daß die im Nabelschnurblut gemessenen Katecholamine fetalen Ursprungs sind und die Plazenta eine hohe Kapazität zur Inaktivierung von freien Katecholaminen aufweist. Die plazentare Extraktionsrate beträgt für NE 77 ± 14%, für E 76 ± 16% und für D 33 ± 25% (Abb. 2). Die bei der Plazentapassage gefundenen nahezu gleichen Extraktionsraten für E und NE weisen in Übereinstimmung mit morphologischen Studien darauf hin, daß in der Plazenta keine sympathische Nervenversorgung vorhanden ist.
2. **Zwischen der NE-Konzentration in der A. umbilicalis und dem APGAR (nach 1 Minute), dem pH und Basendefizit in der A. umilicalis sowie den Veränderungen der FHF (Dezelerationsfläche, basale Herzfrequenz) bestehen hochsignifikante Korrelationen** (Abb. 4–6). Die nähere Analyse der FHF-Veränderungen zeigt (Abb. 7), daß eine Zunahme der Dezelerationsfläche allein ohne Tachykardie nicht mit einem Anstieg der NE-Konzentration korreliert. **Erst bei zusätzlichem Auftreten einer Tachykardie, die zumeist**

mit einer Einschränkung der Oszillationsamplitude einhergeht, ist ein signifikanter NE-Anstieg nachweisbar. Für die E-Konzentrationen in der A. umbilicalis als Ausdruck der gesteigerten adrenalen Freisetzung des Hormons bei Streßzuständen lassen sich ebenfalls Korrelationen zu den fetalen Parametern nachweisen; die Korrelationskoeffizienten liegen jedoch niedriger als dies für NE zutrifft (Abb. 4–6). Die fetale Hypoxie hat auf die arteriellen und venösen D-Spiegel indessen kaum einen Einfluß.

3. Der $tcpO_2$ schwankt in den letzten beiden Stunden vor der Geburt zwischen 0 und 25 mmHg (Abb. 8). In den meisten Fällen liegt der $tcpO_2$ niedriger als der arterielle pO_2 (arterielle-transkutane pO_2-Differenz). Der $tcpO_2$ ist neben der Epidermisdicke und möglichen Meßartefakten (z. B. Druck auf die Elektrode) im wesentlichen abhängig von der Hautdurchblutung. **Offensichtlich kann eine Vasokonstriktion der Hautgefäße, bedingt durch NE-Freisetzung während der Hypoxie, zu einem $tcpO_2$-Abfall führen.** Dafür spricht, daß zwischen hypoxisch bedingter NE-Ausschüttung und dem $tcpO_2$ eine enge Korrelation vorhanden ist: bei steigender NE-Konzentration fällt der $tcpO_2$ ab und die arterielle-transkutane pO_2-Differenz nimmt zu (Abb. 9, 10). Die Stimulation des sympathoadrenalen Systems bei Hypoxie führt zu einer peripheren Vasokonstriktion, die zu der bei schwer deprimierten Neugeborenen bekannten Hautblässe führt (sogenannte „blasse Asphyxie").

Klinische Schlußfolgerungen

Aufgrund des gesicherten Zusammenhangs zwischen erhöhter Katecholamin- (besonders NE)-Sekretion und den verschiedenen diagnostischen Hypoxieparametern der fetalen Intensivüberwachung ist ein hypoxischer Schockzustand des Feten anzunehmen, wenn

- breite und tiefe Dezelerationen mit großer Dezelerationsfläche in Kombination mit Tachykardie,
- eine schwere metabolische Azidose des Feten,
- ein auf wenige mmHg erniedrigter $tcpO_2$ (Artefakte ausgeschlossen)

vorliegen.

Schlüsselwörter: Adrenalin, Dopamin, Extraktionsrate, fetale Herzfrequenz, fetaler Schock, kardiovaskuläres System, Katecholamine, Noradrenalin, transkutan-arterielle pO_2-Differenz, transkutaner pO_2.

Résumé

Catécholamines chez la parturiente, dans le sang veineux maternel et dans le sang ombilical artériel et veineux
On a déterminé les taux d'Adrénaline libre (A), de Noradrénaline (NA) et de Dopamine (D) par une méthode radioenzymatique chez 34 parturientes, dans le sang veineux maternel, et dans les sangs veineux et artériel ombilicaux. Cette étude a été réalisée afin de rechercher la relation entre les catécholamines fœtales et l'hypoxie, le rythme cardiaque fœtal (RCF) et la pO_2 transcutanée (pO_2 tc). On a aussi calculé le taux d'extraction des catécholamines placentaires.

Résultats

1. **Les concentrations de NA (10,200 pg/ml) et de A (1,120 pg/ml) du sang artériel fœtal sont très élevées avec une augmentation de plus de 4 fois des valeurs moyennes par rapport aux valeurs de la veine ombilicale. Comparées aux valeurs du sang veineux maternel, les valeurs de NA sont augmentées de 20 fois, et les valeurs de A de 10 fois** (Fig. 1). Les concentrations de D libre dans le sang artériel fœtal (130 pg/ml) sont élevées 2,5 fois au dessus des taux maternels.
Ces résultats suggèrent que les catécholamines mesurées dans le sang du cordon sont d'origine fœtale et que le placenta a une capacité élevée d'inactivation des catécholamines libres. Le taux d'extraction placentaire est de 77 ± 14 % pour la nor-adrénaline, de 76 ± 16 % pour l'adrénaline, et de 33 ± 25 % pour la D (Fig. 2). Les taux d'extraction placentaire sont virtuellement identiques pour l'adrénaline et la nor-adrénaline; en accord avec les études morphologiques, ces résultats démontrent l'absence d'innervation sympathique au niveau de la face fœtale du placenta.
2. **On a trouvé des corrélations hautement significatives entre les concentrations artérielles fœtales de NA et le score d'APGAR à une minute, le pH et le base déficit artériel ombilical, et les altérations du RCF (surface de décélération, rhythme de base)** (Fig. 4–6). En outre, l'analyse des altérations du RCF (Fig. 7) met en évidence qu'une augmentation des surfaces de décélérations sans tachycardie n'est pas corrélée avec une augmentation artérielle fœtale de NA. **Une élévation significative de NA n'a été trouvée qu'avec une tachycardie surajoutée, tachycardie souvent accompagnée d'une perte de l'amplitude des oscillations.**
On a trouvé que les concentrations artérielles fœtales d'A sont corrélées avec les paramètres fœtaux indiquant une sécrétion surrénalienne hormonale augmentée au cours du stress fœtale. Toutefois, les coefficients de corrélation sont plus faibles que ceux obtenus pour la NA (Fig. 4–6). On n'a pas pu démontrer d'effet significatif de l'hypoxie fœtal sur les niveaux artériels et veineux de D.
3. La pO_2 tc varie de 0 à 25 mm de Hg pendant les deux dernières heures qui précèdent l'accouchement (Fig. 8). Dans de nombreux cas la pO_2 tc est plus basse que la pO_2 artérielle. A côté de l'épaisseur de l'épiderme et des artefacts, la perfusion cutanée est un facteur majeur influençant la pO_2 tc (différence de la pO_2 artérielle transcutanée). **La vasoconstriction des vaisseaux cutanés induite par une élévation de la sécrétion de NA au cours de l'hypoxie peut entraîner objectivement une chute de la pO_2 tc.**
Cette hypothèse est renforcée par la démonstration que la pO_2 tc est corrélée avec la concentration artérielle fœtale de NA: la pO_2 tc diminue lors de l'augmentation de NA et la pO_2 tc artérielle augments (Fig. 9–10). La stimulation du système sympathique pendant l'hypoxie entraine une vasoconstriction

périphérique, vasoconstriction dont témoigne la pâleur des nouveaux-nés déprimés («asphyxie planche»).

Conséquences cliniques

Dans l'optique de la corrélation démontrée entre l'augmentation de la sécrétion de catécholamines (NA) et les divers paramètres de la surveillance du fœtus en cours de travail, on peut considérer qu'il existe un choc fœtal hypoxique si:

- surviennent des décélérations larges et profondes avec une augmentation des surfaces de décélérations, accompagnées d'une tachycardie;
- il existe une acidose métabolique fœtale sévère;
- la pO_2 tc s'abaisse à quelques mm de Hg (en dehors de tout artefact).

Mots-clés: Adrénaline, catécholamines, choc fœtal, différence de la pO_2 artérielle transcutanée, dopamine, nor-adrénaline, pO_2 transcutanée, rythme cardiaque fœtal, système cardio-vasculaire, taux d'extraction.

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