

Some Future Aspects within Perinatal Medicine considered by a Senior Fellow

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ABSTRACT

During the last six decades, a unique new field of applied medicine has been brought forward in the phase before the great biological event of birth, namely into the intrauterine space. On the basis of experiences collected during this time, a few selected thoughts about further aspects based on new but also on some old achievements are presented.

The first one concerns the hardly necessary too frequent use of antibiotics with its negative side effects, such as damage of intestinal flora. We found convincing results in a group of cases with premature rupture of membranes, using PVP-iodine solution for vaginal rinsing to practice in this way an efficient local antiseptic therapy until birth. Another example is amnioscopy, unfortunately replaced to a large extent. But its use remains appropriate because of the low expense and high safety of this method.

A current progress of great importance for the future is the field of perinatal programming. Malprogramming via epigenetic mechanisms results in a lifelong disposition for overweight, obesity, and diabetic metabolic disorders across generations. Important progress and reduction of risks in later life can be expected by suitable research.

A fascinating new field is fetal neurology. Fetal behavioral patterns diagnosed by four-dimensional (4D) ultrasound are directly reflecting developmental and maturational processes of the fetal central nervous system. Such information will hopefully be of great value for further elucidation of neurological problems, for instance, cerebral palsy.

And finally a field in which we have been involved in the 1980s concerns the compensatory intrauterine supply of malnourished fetuses.

Fortunately, there are some efforts to continue these studies to treat severe placental insufficiency with amino acid and glucose by intraumbilical supplementation via a port system.

Keywords: Amnioscopy, Fetal neurology, Perinatal programming, Supply of malnourished fetuses, Vaginal antiseptics.

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Before the start of some selected thoughts, let me remind you that our generation has the great opportunity to be witness to the creation of a new medicine that started at the beginning of the 1960s.

For the very first time, the application of human medicine has been brought forward in the phase before the great biological event of birth, and also in a new widely unknown region, namely in the intrauterine space.

We should be aware that since the beginning of our obstetrical profession, the most impressive evolutionary event was the great change from the predominantly mother-oriented obstetrics with its considerable amount of operative character to combined embryo- and fetal-oriented obstetrics. Before the 1960s, very little – nearly nothing – could be known before birth with regard to the following questions: what is the infant's condition, what is its state of health, and in what state will it be born. But from the 1960s onwards, the fetus became a real patient, in addition to its mother.

The whole field including the first period of life after birth has grown explosively to a huge medical field so that in the meantime we have a "Textbook of Perinatal Medicine" available with more than 2,000 pages, and also several other books which cover self-contained areas within Perinatal Medicine.

It is of course a satisfying feeling for me having worked now for nearly 60 years in the scientific and clinical field of our special new medicine and being now as before active.

On the basis of my so long collected experiences, I will try to present a few of my selected thoughts about further aspects based on new but also on some old achievements.

When we look into the future, we should not concentrate our enthusiasm too much on new recent techniques and methods. We should also critically look back what from the attempts in the past has not been appropriately used for efficient practical clinical benefit and what should be reassessed.

Let me mention two examples out of my field of activities.

The first: Many of our colleagues use antibiotic therapy much too often and unnecessarily ignore its negative side effects, such as damage of intestinal flora which is of considerable importance for immunological reasons. We need a well-functioning immunological state

particularly for resistance against infections which are a frequent cause of preterm birth.

We found convincing results published in 1981¹ in a study of cases with premature rupture of membranes using PVP-iodine solution for vaginal rinsing to practice in this way a very efficient local antiseptic therapy. In 81 cases of PROM, no premature infant died as a result of infection compared with 77 prematures without vaginal infection prophylaxis when 6.5% died.

I think with modern solutions without iodine, such as Octenisept and with more comfortable application, for instance using vaginal suppositories, in the future this could be a much more progressive solution than the blind use of antibiotics with all its negative side effects.

Another example is amnioscopy which can still be of value particularly in postterm cases. Amnioscopy – developed by us in 1961 – is a simple endoscopic examination which takes only a few minutes.² Currently, the most important indication is postmaturity.

The last four decades have seen a considerable change in the monitoring of the fetus during late pregnancy particularly in postterm cases. New methods have been introduced, such as cardiotocography and ultrasonography. They have replaced amnioscopy to a large extent. This is not quite justified. Its use remains appropriate because of the low expense and high safety of this method.³ In contrast to cardiotocography which mainly allows diagnostic insights at the present state, amnioscopy enables a high prognostic safety for at least 48 hours when amniotic fluid is clear. Therefore, this method should be used alternately in combination with cardiotocography every second day and also allows reducing the frequency of more expensive Doppler controls.

Our results: When we performed amnioscopy in the first 2,437 higher risk cases, only 1 fetus (0.04%) died in the antepartum period, when amniotic fluid was clear. Consequently, amnioscopy is a very safe method for differentiation between fetuses at low risk with clear amniotic fluid and at higher risk with green amniotic fluid.

Meconium discharge is an early sign of increased risk. The evidence for this: In 176 cases shortly after meconium has been detected amnioscopically, we ruptured the membranes and took fetal blood samples. Only in three cases, a slight metabolic acidosis was present.

Final conclusion: Amnioscopy should now as before be used either in combination with cardiotocography and Doppler-diagnostics preferably in cases of postterm pregnancy, or alone when the other methods are not available, for example, in developing countries.

Let us now look at new promising achievements which may be of considerable importance for the future.

A current progress of great importance is the field of perinatal programming, particularly concerning overweight and obesity.

Here we rely on a publication of Jens Stupin,⁴ a younger colleague from Charité, Berlin, cooperating with us.

Perinatal programming has meanwhile been established as a field of research for dealing with the impact of the intrauterine and early postnatal environment on fundamental mechanisms of health and disease. The main focus is the phenomenon of an epigenetic, maternal–fetal transmission of acquired conditions. Perinatal malprogramming may also involve the central nervous regulatory centers of metabolism and body weight control. Thus, maternal overweight and/or maternal diabetes (hyperglycemia) during pregnancy and early postnatal overnutrition lead to increased insulin, glucose, protein, and/or leptin levels during critical development stages (e.g., fetal hyperinsulinism). Malprogramming via epigenetic mechanisms results in a lifelong disposition for overweight, obesity, and diabetic metabolic disorders across generations. So for the future, many fields of human medicine can expect important progress in reduction of risks in the later life.

Another fascinating new field is fetal neurology. Here I am grateful for the support from Prof. Asim Kujak who together with Prof. Ritsuko Pooh are pioneers.⁵

One of the greatest challenges of obstetrical ultrasonography is the better understanding of the fetal neurological function. Neurological problems such as cerebral palsy are poorly understood and often falsely attributed to intrapartum events, while for the majority of cerebral palsy cases, it has been proven that the causative pathway starts long before delivery. Several attempts have been made in order to define normal and abnormal fetal neurological function and to develop a method of assessment of the integrity of the fetal nervous system, but still without satisfactory sensitivity.

Fetal behavioral patterns are directly reflecting developmental and maturational processes of the fetal central nervous system. It has been suggested that the assessment of fetal behavior during different periods of gestation may provide valuable information about normal and abnormal brain development, and contribute to the early diagnosis of various structural or functional neurological abnormalities. The introduction of three- and four-dimensional ultrasound (3D and 4D) allowed real-time assessment of fetal behavior. Details of the fetal face, and especially movements of mouth, eyes (facial expressions), and fingers, have been made possible with the introduction of 4D ultrasound. Kurjak Antenatal Neurodevelopmental Test (KANET) is the first method that attempted to use 4D ultrasound in order to assess and combine parameters of fetal behavior and form a scoring system that would assess the fetus in a comprehensive and systematic approach, in the same way that neonatologists perform a neurological assessment in

newborns during the first days of their life, in order to determine their neurological status. KANET appears to be able to identify functional characteristics of the fetus that predict normal and abnormal neurological development, and hopefully future results of the prospective multicentric studies that are taking place at the moment will provide more information on fetal neurology in the next few years. Such information will be of great value in counseling mothers with high-risk pregnancies, like for example in cases when a previous child had cerebral palsy and will also provide valuable evidence for cases of litigation.

Let me finally also mention an interesting field in which we have been involved in the 1980s. It concerns the compensatory intrauterine supply of malnourished fetuses. In 1988, we had the idea to supply malnourished fetuses using a subcutaneously implanted capsula in the abdominal wall of mother on which a catheter was connected. The other end of the catheter was placed in the amniotic cavity or in the abdominal cavity of the fetus (Fig. 1). From both places, absorption of infused substances has been proved.⁶

Because of lack of enough financial support, we had to stop this study. Fortunately, for several years, Prof. Tchirikov from the University Department Halle (Germany) has been continuing these studies based on our idea. His study aims to treat severe placental insufficiencies with amino acid and glucose by intraumbilical supplementation via a port system and hyperbaric oxygenation (Fig. 2). His present conclusion is that the subcutaneously implanted perinatal port system can be used for a long-term intraumbilical administration of nutrients, blood, and other medicine in humans.⁷ The intravascular treatment of growth restriction with fetal nutrition and hyperbaric oxygen could prolong pregnancies with

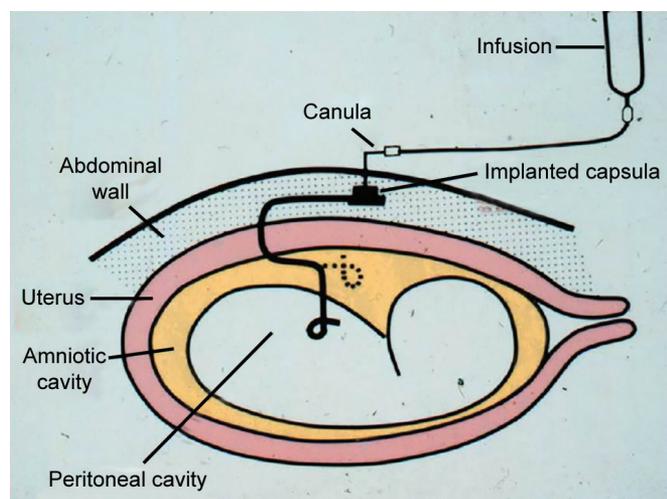


Fig. 1: Our initial concept for a compensatory supply of malnourished fetuses

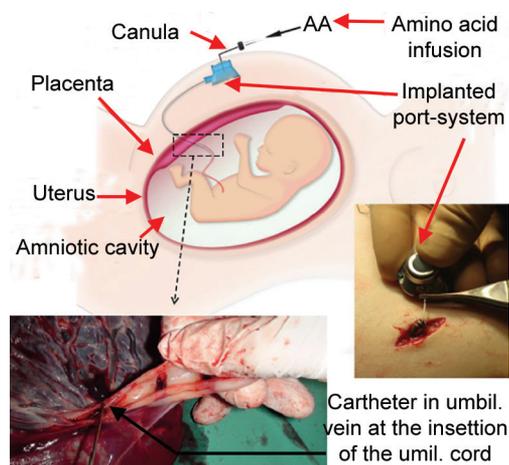


Fig. 2: Tchirikov's system for intraumbilical supplementation

severe placental insufficiency and brain sparing for many weeks. The intraumbilical infusion seems to improve the placental blood perfusion. The commercial amino acid nutrition formulas cannot be safely recommended for the prenatal supplementation of extreme preterm intrauterine growth restriction fetuses because of the lack of some amino acids combined with extreme deviations to this in similar fetuses under physiologic conditions.

Perinatal medicine has in the meantime grown into a huge field with a fascinating dimension and I hope that this small selection of only a few aspects can find some interest.

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