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Ultrasound Assessment of Fetal Growth and Prediction of Birth-date in Late Pregnancy

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Abstract

New clinical method to estimate the intra-uterine fetal weight and predict birth-weight by use of ultrasound and biochemical measurements in the third trimester is presented, even without taking into account calendar gestational age at examination. Estimation is based upon a computerized program for prediction of individual birth-date, automatically differentiating fast, regular and slow growing fetuses as well as indicating physiological and pathological development of the individual pregnancy. Its essential elements are:

1. Identical consideration of ultrasonographics, biochemical and even behavioral (e.g. Ballard-Klimek physical and neuromuscular score of fetal age) data;
2. concurrent comparison of angular increase of the analyzed parameters, with some of them eventually excluded in case of non-congruence;
3. recognition that perinatal clinical data (mean ± SD) of the newborn and mother is obligatory for the entire 6 week range of normal birth occurrence, and not just for the mean date, i.e. only the most probable date (in fact less than 5 % of all deliveries);
4. establishing congruity of predicted values with the actual calendar duration of gestation confirms a normally developing pregnancy;
5. isolation of individual profile as indicative of of abnormal fetal growth, just as abnormalities in many parameters means abnormal development of the pregnancy, and conversely, normal pro-

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Invited paper

files obtained from pregnancies complicated by neurohormonal gestosis, diabetes, hypertension, etc. indicate effective treatment of these co-existing diseases.

In conclusion current imaging modalities have to predict the birth date in days, instead to theretofore ± 3 weeks intervals. It is sufficient to assess in which of six weekly intervals or three bi-weekly periods any evaluated infant has to be born within normal birth occurrence range (from $37^{0}/_{7}$ weeks to $43^{2}/_{7}$ weeks) for all those with the same last menstrual or conceptional date.

Zusammenfassung

Es wird eine neue klinische Methode zur Einschätzung des intrauterinen fötalen Gewichts und zur Vorhersage des Geburtsgewichts durch Verwendung von Ultraschall und biochemischer Meßwerte im dritten Trimester dargestellt, die sogar auf die Berücksichtigung der kalendarischen Dauer der Schwangerschaft zur Beurteilung verzichten kann. Die Einschätzung beruht auf einem Computerprogramm zur Vorhersage des individuellen Geburtstermins, wobei automatisch zwischen schnell, normal und langsam wachsendem Föten differenziert wird und ebenso die physiologische oder pathologische Entwicklung der Schwangerschaft angezeigt wird. Die wesentlichen Elemente sind:

1. Gleichzeitige Beachtung der Ultraschalldaten, der biochemischen Meßwerte und der Verhaltenseinschätzungen (insbesondere nach dem Ballard-Klimek-Meßinstrument der körperlichen und neuronalen Entwicklungsdaten);
2. fortlaufende vergleichende Analyse der Daten, um Fehldaten ausschließen zu können;
3. Beachtung der Tatsache, daß die Normalverteilung für den „normalen" Geburtstermin sich über 6 Wochen erstreckt und sich nicht nur auf ein fiktives Durchschnittsdatum bezieht (Tatsächlich finden nur 5 % aller Entbindungen am errechneten Termin statt);
4. bei Übereinstimmung der vorhergesagten Werte mit den kalendarischen Daten bestätigt dies eine normale Schwangerschaftsentwicklung;
5. das individuelle Profil kann Hinweise auf Abweichungen in der Entwicklung der Schwangerschaft geben und ebenso kann eine Normalisierung des Entwicklungsprofils bei Vorliegen von Erkrankungen wie Gestose, Diabetes, Bluthochdruck, usw. die Wirksamkeit einer Behandlung anzeigen.

Zusammenfassend kann man behaupten, daß mit Hilfe der von uns ausgearbeiteten Computerverarbeitung der Daten eine Voraussage des biologischen Geburtstermins auf Tage möglich ist, statt wie bisher auf Wochen.

Introduction

Accurate knowledge of fetal growth and maturation is essential for high quality prenatal care. The rate of fetal development is greatest just after fertilization and then continues to decline not only until birth, but also until the puberty growth spurt. The greatest developmental increase is at first demonstrated by head diameter, followed by body length, placental mass and finally fetal body mass. It is easiest to demonstrate this with changes in body parameters of the fetus. Nevertheless, too often the observed variability in developmental rates is fallacious, since the planar, square and cubic dimensions used in their description are reduced to linear functions in calendar, instead of biological time [19–25].

Progress has recently been made in implementing computerized techniques that can be used e.g. to obtain magnetic resonance images (MRI) in a fraction of a second rather than in minutes [20]. What is more, MR images can recflect almost immediately a multitude of parameters, in contrast to the spatial distribution of a single parameter provided by acoustic (ultrasoung), electron density (computed tomography), or isotope density (nuclear scanning) modes. Thanks to MRI, the planar square and cubic dimensions used in the description of fetal growth development no longer need to be reduced to linear functions. This is especially important since man is born all year long in any consecutive month or week with practically the same average birth weight and length as well as a constant average gestational calendar age (281 days) with at least a range of $\pm$ 3 weeks. This was confirmed also by ultrasonography [1, 6–9, 11, 12, 27–32].

As a final result, the dependence on a single measurement to assess gestational age has a 95 % confidence interval of $\pm$ 3 weeks or more in the third trimester, but it could not be better than in... Nature! This undoubtedly was documented just prior to the clinical application of ultrasound [5, 13, 14, 18, 19, 26] although already known previously from Aristotle's statement "All creatures have their determined time for giving birth and carrying fetus, only man is born all year long, not in determined time, one in the seventh month, the other in the eight, and so on till the beginning of the eleventh month".

Clinical Assessment of Fetal Development

In spite of clinical data, the ultrasonographers are still using cross-sectional methods or scales of calendar gestational age in assessment of pregnant women. In consequence, the confidence intervals for any fetal ultrasound measurement increase with advancing gestation. Therefore all results given by USG machines encompass not only mean values, with an accuracy in days (e.g. 35 weeks 2 days), but also their standard deviations or ranges in weeks (e.g. 35 weeks 2 days $\pm$ 2 weeks), which is overlooked by doctors. For example, what ultrasound data: *35 (33–37) weeks* signifies is that there is a 95 % chance the age is between 33 to 37 weeks and that only the most likely age is 35 weeks. This is particularly important in late gestation and may have psychological as well as legal implications.

Any fetal measurement is conditioned by biological development of pregnancy. This means that not calendar, but biological age is a decisive predictor of obtained values. Therefore all obstetrical and especially ultrasonographic books,

scales and diagrams have to encompass all pregnant women, including also those beyond the average length of human pregnancy, i.e. 40 weeks' gestation. Since the time of the great mathematician C. F. Gauss from Göttingen, a statistical method is known, in which the standard deviation about the mean of a statistical sample depends on the distribution of frequencies of selected variables, e.g. length, weight, maturity.

During the years 1926 to 1946, at Göttingen, eight thousand physiological pregnancies were evaluated by H. Hosemann et al. [14] according to the following criteria: birth date (decade), month of birth, hour of birth, parents constitutional type, status of the family, the burden of manual labor and socioeconomic conditions, maternal nutrition, maternal age, number of previous pregnancies and the mother's menstrual cycle. Presented by them, the frequency distribution of durations of gestation is based exclusively on clinical criteria of maturation; such as length of nails, color and thickness of skin, development of hair, among others, However, from these criteria alone, one is not able to separate the regular from the irregular gestational periods. The distribution curve of variables, its shape like a bell, has its peak directly over the average value (the mean). This is the most frequently observed mean time span from the last menstrual period until birth. From this peak value, the curve falls off symmetrically toward either extreme, such that a shorter or longer interval will be encountered with equal probability. On this 281st day, they observed the occurrence of only 4.46 % of all births. Therefore, from the bell shaped graphs one can not deduce when within a period of $37^{0}/_{7}$ to $43^{2}/_{7}$ weeks from the last menstruation, birth of the mature neonate takes place.

Biological age accounts for the maturation of a fetus similarly to other dimensions of mass or volume, whereas calendar age only reflects the number of days, weeks or months that a pregnancy has progressed. That is why, it became necessary to modify also contemporary methods of interpreting ultrasonography data. First of all, from the medical and ethical point of view, we had to be opposed to the "obstetrical scale" consisting of sequential periods: pre-, at- and post-term. This is an incorrect method of dating the development of pregnancy. Term is really the point of maturation of an individual fetus within the normal range of birth occurence (postmenstrual $37^{0}/_{7}$–$43^{2}/_{7}$ weeks). True preterm refers to a neonate born before its point of maturation (premature baby) and true postterm refers to a neonate born after its individual point of maturation (postmature baby), and nothing more!

The linear period of fetal growth begins at 28 calendar gestational weeks with a steady incremental average weight gain of about 1.1 kg every 6 weeks continuing until 18 weeks postnatally [10, 14, 29, 33]. There are very high, statistically significant correlation coefficients of various fetal ultrasound measurements (alone or in different combinations) with biological gestational age. Therefore, if the obstetric data on gestational calendar age is questionable, clinical assessment of neonatal maturity is preferred [10].

For example, the Ballard Maturation Score is a valid and accurate assessment tool for precise interpretation of the degree of fetal maturity [2–4], but not of the calendar length of gestation, especially beyond 36 weeks [24]. In six neuro-

logic (posture, square window, arm recoil, popliteal angle, scarf sign and heel to ear) and six physical (skin, lanugo, plantar creases, breast, ear and genital) criteria correlate only with individual gestational age. It is well known that some fetuses reach full maturity just after 37 weeks while others at the 40th or even 43rd week (Fig. 1). In spite of this, Ballard scores are different; only newborns at 44 weeks have scores of 50 while newborns with shorter length of pregnancy have lower score values, e.g. 40 at the 40th week, and 33 at the 37th week. Even meta-analysis of J. L. Ballard papers showed that within a period between 37 and 43 weeks, there is the same distribution of mature newborns [23]. So, regardless of fetal weight and length, the Ballard score informs only about the degree of fetal maturity. Therefore it was reasonable to propose a constant distribution of scores: 39 ± 3 points within a period from 37 0/7 to 43 2/7 weeks [16, 17], while at the 28th week: 10 ± 2 points [24]. This own interpretation takes into consideration the relative length of pregnancy in the individual child (Ballard-Klimek maturation rating score – Fig. 2) instead of theretofore used J. L. Ballard rules (Fig. 1) that only newborns at 44 weeks can have scores of 50, while infants with shorter length of pregnancy have lower values.

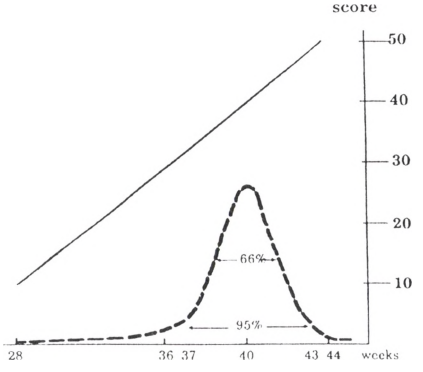

Fig. 1. Ballard maturation rating to Gaussian distribution of births [23].

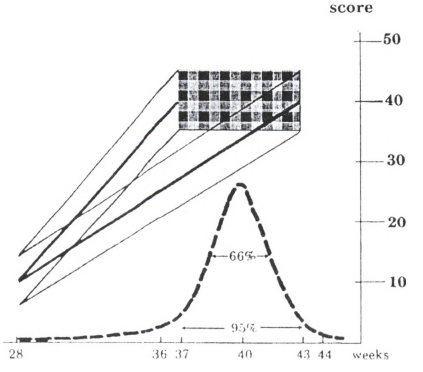

Fig. 2. Ballard-Klimek maturation rating to Gaussian distribution of births [23].

Together, all the above may be summarized by the conclusion, derived from our latest clinical data of 1200 unselected, successive, single fetus vaginal births with newborn body mass > 2500 g [16, 17]. On the date of birth a mature newborn was characterized by the following average values (± SD); body mass 3412±429 g (range: 2530–5200 g), body length 54 ± 3 cm (range: 42–65 cm), 1 minute Apgar 9.8 ± 0.5 (range: 7–10) and Ballard-Klimek scores 39 ± 3 (range: 23–50). It is natural that slow maturing infant may become large, average or small at birth just as fast or regular developing ones. Figure 3 shows number of infants weighing > 2500 g, born in consecutive weeks with the corresponding degree of their maturation. Figure 4 demonstrates the percentages of premature, mature and postmature newborns in consecutive weeks. The above data indicates a natural

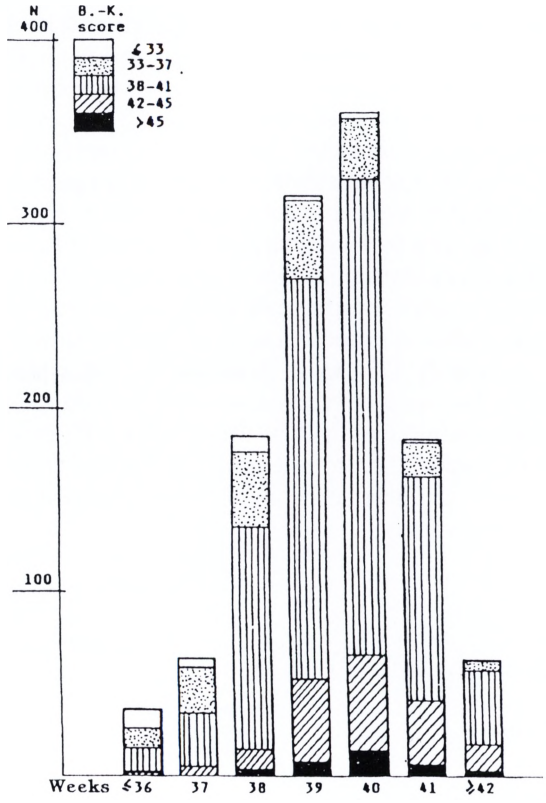

Fig. 3. Number (N) of infants weighing > 2500 g, born in consecutive weeks with the corresponding degrees of their maturation (Ballard-Klimek scores).

Gaussian distribution of deliveries with decreasing absolute (Fig. 3) and relative (Fig. 4) frequencies of less mature newborns, especially below 37 B & K scores in longer lasting pregnancies, and vice versa – with increasing number of more mature newborns, especially > 42 scores.

Taking into account the normal distribution of the above data, one may consider the body mass, body length, 1′ Apgar and Ballard-Klimek scores of two newborns: one with respective values: 2500 g, 50 cm, 8, 33 and the other with values: 4500 g, 56 cm, 10, 45. Both are of equal maturity, that is have identical biological age, in which time is a dimension, as the fundamental condition of their maturation. In the mature newborns, just as body length or mass, this dimension of maturity time as well is contained within ± 2 SD from 259 days (37 $^{0}/_{7}$ weeks) to 302 days (43 $^{2}/_{7}$ weeks). Simply stated, some fetuses mature at a faster rate than others. This does not imply that those maturing faster, will be larger or maturer, and vice versa (Figs. 3, 4). Yet this conclusion has a very significant obstetrical implication for the proper evaluation of the LMP date. The parameters of interest to us will be measurable several weeks later, it means from or after conception, in the evaluation of fetal growth and maturation as a real goal of pregnancy. As apparent from the attached diagram (Fig. 5), with advancing postmenstrual or postconceptual maturation of the fetus depending

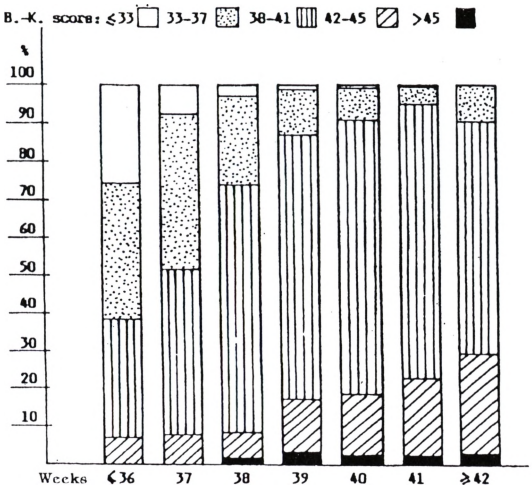

Fig. 4. Percentage of premature (B & K scores ≤ 33, mature (33–45) and postmature (> 45) newborns in consecutive weeks of births occurrence.

upon its rate (fast, regular or slow) and final growth outcome at delivery (large, average or small newborn), these values become more convergent. Of course, in contrast to this biological scale, parameters are divergent when the only point of reference is taken to be the date of the LMP or conception on the calendar scale (Fig. 6), which cause common place ultrasonographer's mistakes.

Disregarding time as a developmental dimension from one side and using only calendar scale of time on the other – ultrasonographers are unable to eliminate the sigmoidal portion of fetal growth curves in late pregnancy. One should not forget, that beginning after 37 weeks there is not a continuum of all birth occurrences, but separate, individual births in consecutive weeks of newborns whose life started at the same time, i.e. their conceptions occurred at the same day. At delivery each newborn according to its own rate of maturation (fast, regular or slow) has ended fetal life in one of six different weeks. In each final week any newborn has its individual growth and maturation values which together are giving the mean $\pm$ SD characteristic of their week of delivery. The small differences in average values between consecutive weeks most likely result from the maternal factors, which for example cause early or later onset of labor. It is why in each week of birth occurrence any pregnancy has to be identically diagnosed and managed. Therefore one may not ultrasonographically (as by any other means) evaluate differently infants to be delivered at 37 to 39 weeks from those from 40 to 42 weeks. This particularly concerns terminating each so called postdated (postterm) pregnancy only after calendar 42 weeks, while fully mature infants just exist in weekly group with shorter maturation period.

The basic problem in establishing connections between neonatal and theretofore prenatal measurements of maturation was that the latter one had only been measured after birth. A new clinical method to estimate the intra-uterine fetal growth and predict birth-date by use of ultrasound and biochemical measurements in the third trimester is now possible, even without taking into account calendar gestational age at examination [15, 22–25]. Estimation is based upon a computerized program automatically differentiating fast, regular and

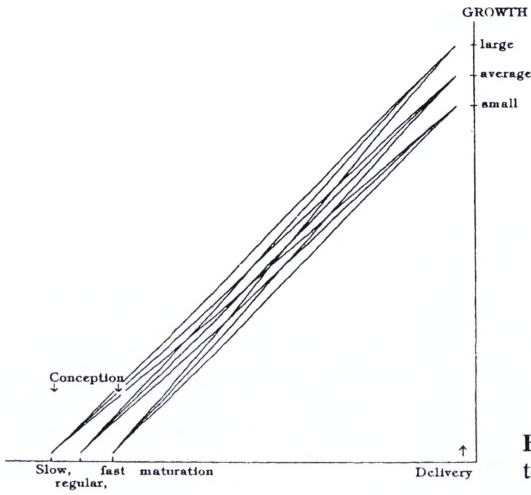

Fig. 5. Fetal growth and maturation to biological gestational age.

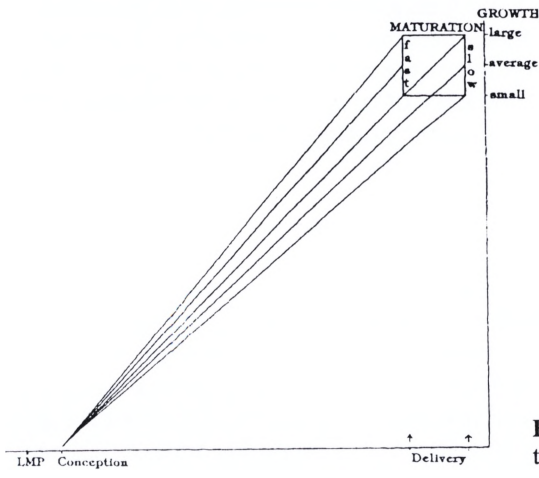

Fig. 6. Fetal growth and maturation to calendar gestational age.

slow growing fetuses as well as indicating physiological and pathological development of the individual pregnancy. What is more, the universal diagram may serve for preparing biological and calendar scales for all obstetrical parameters (Figs. 7, 8).

Everybody may collect the average birth weight as well as fetal and gestational lengths within consecutive weeks or months at his own department. It is sufficient to collect the appropriate cross-sectional maternal parameters at 28 to 30 weeks gestation and also within the last few days before the onset of spontaneous delivery of a single, healthy newborn. Having such data one has simply to substitute mean values and their standard deviations in the universal diagram for prediction of birth-date (Figs. 7, 8). The degree of fetal maturity and prediction of its birth scores by use of ultrasound may be assumed, if two ultrasound measurements are performed within the interval of at least 15 days (optimum 4–5

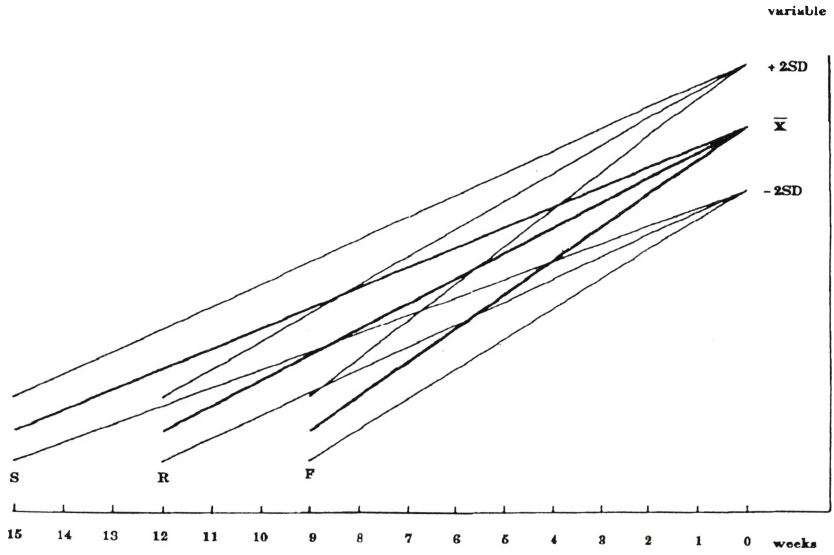

Fig. 7. Slow (S), regular (R) and fast (F) fetal maturation to biological gestational age.

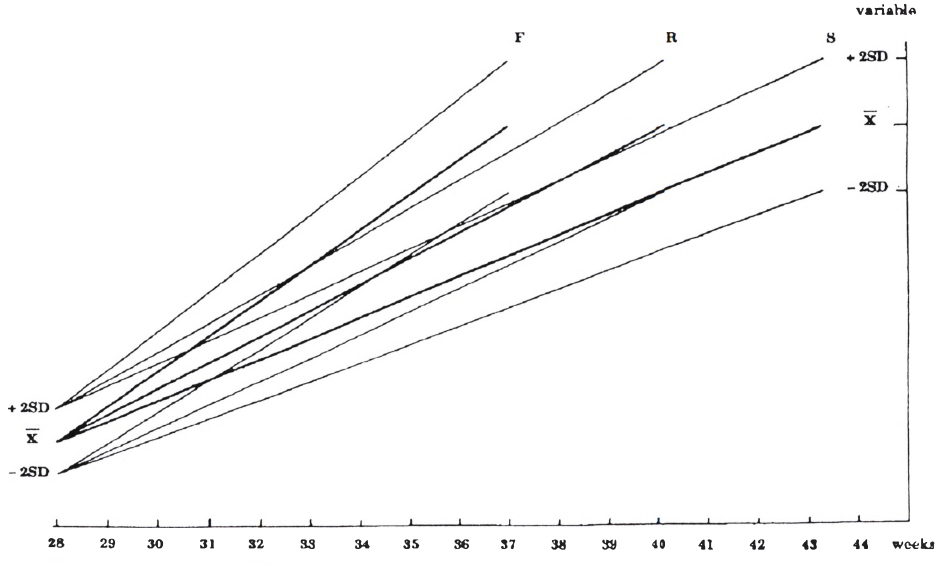

Fig. 8. Slow (S), regular (R) and fast (F) fetal maturation to calendar gestational age.

weeks) beginning at 28 calendar gestational weeks, or one of the measurements was obtained earlier but in this case the date of the last menstrual period (LMP) has to be known.

Fetal parameters can be calculated from AC, BPD, HC and FL independently or from some of them in such combination that into account are taken only correct measurements, with the same accuray of birth prediction. The essence of

computed measurements is that it relies on the analysis of angular increase of the variables in question.

Conclusions

Medicine has to use the proper methods of distinguishing the baby which should be born at the beginning of the normal range from that which should be born at the end of the normal range, or between these limits. Nowadays by completing an individual fetal growth profile (regular, fast and slow) rather than obtaining cross-sectional ultrasonographic data alone, the obstetrician is in a better position to detect not only abnormalities of fetal development. He may also monitor the outcomes of eventual therapeutic interventions and predict the optimal date of childbirth. In some cases medical intervention could be found to be irresponsible if the parents asked the doctor if he had done everything that had to be done from the diagnostic, but not exclusively statistical point of view.

Sonography has had a profound effect on the reported distribution of gestational age. While the characteristics of the obstetric population changed only slightly, the gestational age distribution shifted with a decrease in the mean duration of pregnancy. There was also rise in the reported preterm delivery rate. Some of this rise can be explained by an increase in obstetrical interventions, and some can be explained by changes in the way physicians rounded off gestational age.

Any error of fetal growth or maturity estimation will result from one or more of the following: skill of the ultrasonographer, technical capabilities of the USG apparatus and the type of estimation procedure. For example, the growth function equation describes changes in shape of the average fetal growth curve based upon cross-sectional evaluation of data, instead of longitudinal estimations. Currently at the time of the ultrasound examination, only the expected date of delivery is used. Menstrual age as based on the first day of the last menstrual period is used if an ultrasound exam shows that menstrual age is within $\pm$ 10 percent (in the first trimester) or $\pm$ 10 days (in the second trimester) of ultrasound age. Otherwise, the menstrual age is based on the ultrasound measurements. In either situation if a baby is born three weeks earlier or later than expected in accordance with ultrasound dating, the parents may not become upset, but may choose to persue litigation.

A new clinical method to estimate the intra-uterine fetal weight and predict birth-weight by use of ultrasound and biochemical measurements in the third trimester is possible, even without taking into account calendar gestational age at examination [15, 22–25]. Estimation is based upon a computerized program for prediction of individual birth-date, automatically differentiating fast, regular and slow growing fetuses as well as indicating physiological and pathological development of the individual pregnancy.

The essential elements of the new computer-aided prediction of birth date and fetal growth are:

1. determination of predicted values based upon analysis of singular parameters considered separately;

2. identical consideration of ultrasonographics, biochemical and even behavioral (e.g. Ballard-Klimek physical and neuromuscular score of fetal age) data;
3. concurrent comparison of angular increase of the analyzed parameters, with some of them eventually excluded in case of non-congruence;
4. recognition that perinatal clinical data (mean ± SD) of the newborn and mother is obligatory for the entire 6 week range of normal birth occurrence, and not just for the mean date, i.e. only the most probable date (in fact less than 5 % of all deliveries);
5. prediction of body growth and term of delivery occurs without taking into account the date of the last menstrual period (LMP) or conception;
6. determination of the calendar length of pregnancy without taking into account the LMP and/or conception dates may have medico-legal implications, such as confirmation of paternity or in case of exposure of a pregnant women to detrimental environmental factors or obstetrical procedures;
7. establishing congruity of predicted values with the actual calendar duration of gestation confirms a normally developing pregnancy;
8. isolation of individual profile as indicative of abnormal fetal growth, just as abnormalities in many parameters means abnormal development of the pregnancy; and conversely, normal profiles obtained from pregnancies complicated by neurohormonal gestosis, diabetes, hypertension, etc. indicate effective treatment of these co-existing diseases.
9. normalization of profiles, previously determined to be abnormal based on the examined parameters – allows monitoring the effect of therapeutic interventions;
10. antenatal assessment of Ballard-Klimek values constitute an essential predictor for perinatal procedures and/or treatments of newborns, especially extremely premature infants.

In summary current imaging modalities have to predict the birth date in days, instead to therefore ± 3 weeks intervals. It is sufficient to assess in which of six weekly intervals or three bi-weekly periods any evaluated infant has to be born within normal birth occurrence range for all those with the same last menstrual or conceptual date. The common characteristic of these intervals with relative exception of the 37th week is practically the same possibility of pre-, at- or postmature birth.

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