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## Multifactorial study of the risk of prematurity at 32 weeks of gestation

### I. A study of the frequency of 30 predictive characteristics

Emile Papiernik, Monique Kaminski

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Prematurity is today the most essential problem in obstetrics, particularly if we consider its importance in perinatal mortality, and above all its far-reaching neurological and psychological consequences.

#### 1. Preventive methods are necessary

It is impossible to solve this problem with curative methods only, as, even with the best care, treatment of prematures reduces mortality, but does not eliminate the consequences of the premature birth. It is therefore necessary to turn to preventive methods. But it is not possible to take preventive measures against an unforeseeable accident. The research and improvement of prognostic methods should now be our main concern.

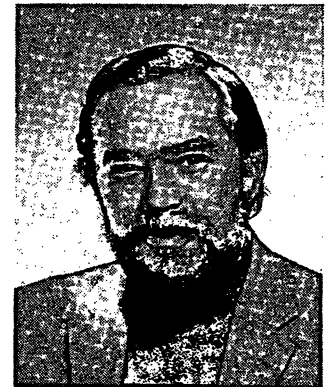
The aim is to be able to predict the risk of a premature birth long before it occurs. Our technique is a scoring method. Of all the cases being supervised in an antenatal care program, we wish to isolate those with the highest risk of prematurity and apply suitable preventive therapy.

Until now, despite very important studies such as RAIHA's [11], it was thought to be impossible or very difficult to predict the occurrence of a premature birth. There are many different etiological reasons for the occurrence of premature birth. All influencing factors have to be considered.

From the results of several studies, we can piece together the different etiological reasons which could shorten the length of gestation and reduce the child's weight [4-12, 16-18]. We tried to

#### Curriculum vitae

EMILE PAPIERNIK-BERKHAUER was born in Paris in 1936. He received his medical degree from University of Paris, and a Ph. D. degree from faculty of sciences in the field of Physiology of Reproduction. He was chief-assistant to Prof. VARANGOT at the Maternity of Port-Royal from 1966 until 1972, when he was called to University of Paris-



Sud as chief of Hospital Antoine Béchère obstetrical-gynecological department. He was one of the first obstetricians to insist on the importance of good prenatal care for the detection and prevention of premature birth and developed a coded method for the evaluation of the risk of premature birth (1969).

find a decisive rule for predicting prematurity using a very simple multi-factorial measure implemented during the course of pregnancy [13, 14].

Our initial etiological study, which we present in this paper, will substantiate our arguments for this method. We have already pointed out [13, 16] the reasons for recording many predictive characteristics during pregnancy (in our study, 30 items) giving each of them a score in order of gravity from 1 to 5 points and then estimating the overall risk from the total number of points accumulated.

This technique, however had only an empirical basis. For validation we applied it to a certain number of women who delivered in 1969, which were recorded retrospectively. A prospective study of prevention has been begun, and the

results for 1970 are being analysed at present. A further study, with repetitive evaluation of risk, is at present in use and under evaluation.

## 2. Methods

We have recorded 30 characteristics during pregnancy which are known to increase the occurrence of premature birth. The list and definition of the characteristics are given in Tab. I. They are grouped according to socio-economic factors, unfavorable obstetrical antecedents, fac-

tors of fatigue, danger signs at examination, and danger signals pointing to imminent delivery. There is also a risk factor, composed of 4 characteristics (long travel, unusual fatigue, etc.) but it was not fully investigated in this retrospective sample.

### 2.1 The sample

We have compared

1) a group of 153 mothers having delivered a child weighing less than 2,500 g, at the Paris

Tab. I. List and definitions of 30 characteristics which are known to increase the occurrence of premature delivery.

#### General and social factors

1. **Unwed mother:** pregnancy of a woman unmarried at the time of the examination.
2. **Low weight:** mother's weight before pregnancy lower than 45 kg.
3. **Diminutive size:** mother's height less than 1.50 m.
4. **More than 2 children without domestic help.**
5. **Unfavorable age:** less than 20 years or more than 40 years.
6. **Low social class:** non skilled workers or precarious financial situation.

#### Unfavorable obstetrical or gynecological antecedents

7. **D and C:** previous D and C for spontaneous or induced abortion.
8. **Uterine malformation:** malformation either diagnosed by hysterography, or evident during the pregnancy (uterus arcuatus, uterus septus, uterus didelphys, hemi-uterus).
9. **Cylindrical uterus:** minor malformation of the uterus; parallelism of the walls of the uterus diagnosed during the pregnancy.
10. **Previous late abortion:** previous abortion from the 3rd to the 6th month of pregnancy (from the 14th to the 28th week).
11. **Previous premature birth:** previous delivery of a child weighing less than 2500 g.
12. **Short interval since last pregnancy:** less than one year between the last delivery and fecundation of the present pregnancy.
13. **Contractibility of the uterus:** Painful contractions also induced by examination, at regular rhythm and of longer duration than the usual spontaneous contractions. This factor is difficult to define exactly without recording the contractions.
14. **Presenting part** lower than 0 or + 1, as far as the level of the sciatic spines.
15. **Thinned lower uterine segment:** very thin and in shape of cupola.

16. **Shortened cervix:** cervix shorter than 2 cm.

17. **Patency of the internal os:** permeable at the internal cervical os.

#### Danger signals at examination

18. **Metrorrhagia during pregnancy:** bleeding during the 2nd or the 3rd trimester of pregnancy.
19. **Suspicion of placenta praevia:** association between metrorrhagia and irregular presentation.
20. **Multiple pregnancy:** confirmed by radiography.
21. **Hydramnion**
22. **Proteinuria**
23. **Hypertension:** systolic > 130 and/or diastolic > 90.
24. **Excessive weight gain:** more than 9 kg at 32 weeks.
25. **Loss of weight during the previous month:** loss of at least 1 kg during the previous month.
26. **Less than 5 kg weight gain:** at 32 weeks of pregnancy.

#### Factors of fatigue

27. **Work outside the home.**
28. **Strenuous work:** for work involving strenuous physical effort, standing, continuous nervous tension. Occupations for women as nurses, telephone operators, punch-card operators, cleaning staff, sales staff, hair-dressers, dentists, etc. are implied.
29. **Apartment above 3rd floor without elevator.**
30. **Long daily commuting-time:** more than 1½ hours daily.

We also use certain terms:

**Stage of pregnancy at examination:** the stage of pregnancy when the signs are recorded, calculated in weeks from the first day of the last menstruation.

**Number of consultations before 6th month:** Number of consultations before the 6th month of pregnancy (before 28th week). The total number is not recorded for it depends on the length of gestation. Only the number of consultations at the obstetrical department of Port-Royal are taken into consideration.

Maternité de Port-Royal in 1969 (in case of twins, a mother was kept in this group if at least one of the children weighed less than 2,500 g); 2) a control group, selected at random, composed of 222 mothers having delivered children weighing more than 2,500 g in 1969, in the same obstetrical department.

## 2.2 Source of data

The information used was collected from the patient medical records completed during prenatal consultation. The data was used to calculate the risk only after delivery, and our technique did not influence the treatment given.

## 2.3 Choice of optimum stage of pregnancy for studying risk

We chose to study the risk at the 32nd week of gestation. This moment seemed suitable, for it takes place 2 or 3 weeks before the delivery of a high percentage of prematures with poor prognosis: before the 32nd week, the frequency is lower, after the 35th week, the danger is not so acute. As all the patients were not examined at exactly this stage of pregnancy, we recorded the results of the clinical examination nearest to the 32nd week.

## 3. Results

Among the 375 cases in the sample, 153 mothers of prematures and 222 controls, the stage of pregnancy was missing for 10 children. These cases were excluded. The calculations were thus made on 149 mothers of prematures and on 216 controls. We studied the distribution of the characteristics in each group. We divided the two groups according to the length of gestation: up to and including the 37th week, 38 weeks and more

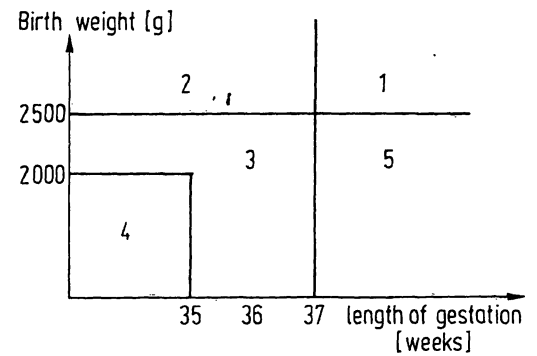


Fig. 1. Characterization of the groups.

for the infants weighing over 2,500 g. The same division into groups was done for the infants weighing less than 2,500 g, and a fifth group was defined, composed of infants with birth-weights under 2,000 g and length of pregnancy less than 36 weeks.

## Definition of the groups (Fig. 1)

- G 1 Length of gestation  
> 37 weeks and weight > 2,500 g 198 cases
- G 2 Length of gestation  
≤ 37 weeks and weight > 2,500 g 18 cases
- G 3 Length of gestation  
≤ 37 weeks and weight ≤ 2,500 g  
and  
> 35 weeks and weight > 2,000 g } 56 cases
- G 4 Length of gestation  
≤ 35 weeks and weight ≤ 2,000 g 46 cases
- G 5 Length of gestation  
> 37 weeks and weight ≤ 2,500 g 47 cases

Tab. II—VI reporting the frequencies of the abnormal characteristics observed at 32 weeks of gestation show most of the variables we have recorded to be relevant.

Tab. II. General and social factors.

| Group                                      | n | G 1<br>198 | G 2<br>18 | G 3<br>56 | G 4<br>46 | G 5<br>47 |
|--|---|------------|-----------|-----------|-----------|-----------|
| Unwed mothers                              | % | 10         | 11        | 14        | 9         | 13        |
| Mother's weight < 45 kg                    | % | 6          | 6         | 5         | 2         | 15        |
| Mother's height < 150 cm                   | % | 1          | 0         | 2         | 0         | 2         |
| More than 2 children without domestic help | % | 3          | 6         | 2         | 13* (a)   | 4         |
| Mother's age < 20 or > 40                  | % | 14         | 22        | 18        | 7         | 13        |
| Low social class                           | % | 12         | 28        | 18        | 31**      | 21        |

Significance \*  $p < 0.05$  \*\*  $p < 0.01$  (a) Chi-square test with YATES' correction

Tab. III. Unfavorable obstetrical or gynecological antecedents.

| Group                               | n | G 1<br>198 | G 2<br>18 | G 3<br>56 | G 4<br>46 | G 5<br>47 |
|-------------------------------------|---|------------|-----------|-----------|-----------|-----------|
| D and C                             | % | 16         | 11        | 25        | 28        | 19        |
| Uterine malformation                | % | 1          | 0         | 0         | 9* (a)    | 0         |
| Cylindrical uterus                  | % | 2          | 0         | 2         | 0         | 4         |
| Previous late abortion              | % | 1          | 6         | 7* (a)    | 13*** (a) | 0         |
| Previous premature birth            | % | 7          | 6         | 18*       | 28***     | 11        |
| Short interval after last pregnancy | % | 5          | 6         | 11        | 9         | 4         |

Significance \*  $p < 0.05$  \*\*  $p < 0.01$  \*\*\*  $p < 0.001$  (a) Chi-square test with YATES' correction

Tab. IV. Factors of fatigue.

| Group                                      | n | G 1<br>198 | G 2<br>18 | G 3<br>56 | G 4<br>46 | G 5<br>47 |
|--|---|------------|-----------|-----------|-----------|-----------|
| Work outside the home                      | % | 77         | 33**      | 64        | 63        | 68        |
| Strenuous work                             | % | 26         | 11        | 37        | 46**      | 36        |
| Apartment above 3rd floor without elevator | % | 3          | 0         | 5         | 2         | 4         |
| Long daily commuting-time                  | % | 8          | 6         | 25***     | 11        | 19**      |

Significance \*\*  $p < 0.01$  \*\*\*  $p < 0.001$

Tab. V. Dangersignals at examination.

| Group                      | n | G 1<br>198 | G 2<br>18 | G 3<br>56 | G 4<br>46 | G 5<br>47 |
|----------------------------|---|------------|-----------|-----------|-----------|-----------|
| Metrorrhagia               | % | 4          | 6         | 4         | 26*** (a) | 4         |
| Placenta praevia           | % | 1          | 0         | 0         | 7         | 2         |
| Multiple pregnancy         | % | 0          | 0         | 11*** (a) | 13*** (a) | 13*** (a) |
| Hydramnion                 | % | 1          | 0         | 2         | 2         | 0         |
| Excessive weight gain      | % | 37         | 17        | 14**      | 17*       | 30        |
| Loss of weight             | % | 1          | 0         | 4         | 2         | 2         |
| Less than 5 kg weight gain | % | 2          | 0         | 11** (a)  | 2         | 9         |
| Proteinuria                | % | 1          | 0         | 0         | 2         | 4         |
| High blood-pressure        | % | 2          | 0         | 5         | 2         | 9         |

Significance \*\*  $p < 0.01$  \*\*\*  $p < 0.001$  (a) Chi-square test with YATES' correction

Tab. VI. Danger signals for imminent delivery.

| Group   | n | G 1<br>198 | G 2<br>18 | G 3<br>56 | G 4<br>46 | G 5<br>47 |
|---|---|------------|-----------|-----------|-----------|-----------|
| Uterine contractibility                       | % | 15         | 22        | 27*       | 63***     | 30**      |
| Presenting part descended lower than 0 or + 1 | % | 4          | 0         | 20***     | 28*** (a) | 11        |
| Thinned lower uterine segment                 | % | 10         | 6         | 27***     | 26**      | 19        |
| Shortened cervix                              | % | 20         | 39        | 64***     | 67***     | 43***     |
| Patency of internal os                        | % | 12         | 28        | 47***     | 61***     | 23*       |

Significance \*  $p < 0.05$  \*\*  $p < 0.01$  \*\*\*  $p < 0.001$  (a) Chi-square test with YATES' correction

We have compared the groups 2, 3, 4, 5, to group 1. Characteristics for which the frequencies in groups 2 to 5 do not differ from that in group 1 are often found to have a low frequency in the sample (for instance height less than 150 cm, perhaps because of a bad choice of the limit for the unfavorable height) or, on the contrary to have too high a frequency (for instance work outside the home, a characteristic too unspecific). The different unfavorable characteristics are found to be more frequent the shorter the gestation and the lower the birth-weight. Moreover, the way the abnormal signs are grouped is different for mothers of prematures and for mothers of dysmatures (i. e. low-birth weight for stage of pregnancy).

#### 4. Discussion

A single clinical examination (here chosen to be near the 32nd week) cannot provide a complete picture of the course of a pregnancy. Some signs for example which are very important later in the pregnancy such as arterial hypertension, do not differ statistically between the groups at the 32nd week of gestation because they still are very infrequent.

However it was important to assess the value of information obtained at a single examination. In a survey being carried out at present, several successive examinations are performed during the pregnancy and we hope that such information will enable us to make a better judgement.

Results in Tabs. I—VI provide an idea of the relationship among the factors and are an aid in preparing a real multifactorial study of the etiology of prematurity, though the small number of cases may suggest lack of significance.

Thus in Tab. III we note that the factors representing unfavorable obstetrical or gynecological antecedents constitute a very important group for G 3 and G 4: "pathology of the cervix or the isthmus", characterized by:

- D and C
- previous late abortion
- previous premature deliveries

and we can interpret this in terms of a dysfunction of the isthmus.

Also for G 3 and G 4, and even G 5 a second group of signs is important, which we defined as "danger signals for imminent delivery" (Tab. VI). It is composed of 5 characteristics: Uterine contractility, presenting part descended, thinned lower uterine segment, shortened cervix, patency of internal os, representing clinical signs known to every obstetrician and recorded here. Their predictive value is very important, even observed singly (e. g. patency of the internal os) and especially if observed long before the expected date of delivery, as in this study, at 32 weeks.

Another group is of interest for predicting prematurity: changes in mother's weight during pregnancy (Tab. V). The table points out the importance of a gain of less than 5 kg. But we observe that the factor "excessive weight gain" is the only one with a much lower frequency in the pathological groups. Thus we find a relationship between a low weight gain, and a shortening of gestation or a low infant birth-weight. These results are in agreement with those of the nutritionists [17].

The group "factors of fatigue" (Tab. IV) is found in mothers with a shortened length of gestation as well as in those of mature but low birth-weight children, and hence must be retained.

Finally, the results point out that **the characteristics influencing intrauterine growth retardation form a different group from those**

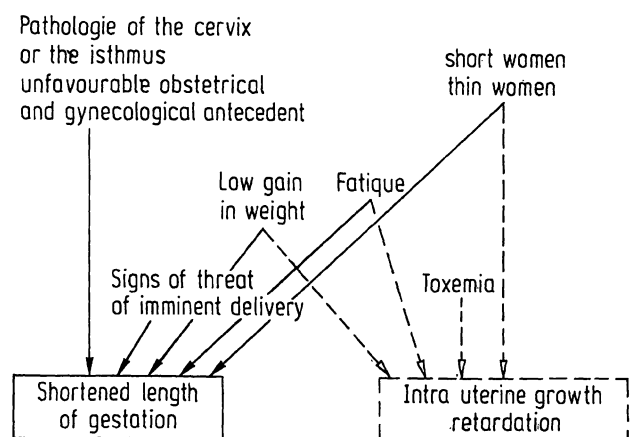


Fig. 2. Diagram of the principal factors of prematurity or intrauterine growth retardation. Low socio-economic level, indifference, low number of consultation increase the risk.

**demonstrativ prematurity.** Here, diminutive height of mother, mother's low weight (Tab. II), gain in weight less than 5 kg, seem to be very important; of course, we find also the factor toxemia, with hypertension and proteinuria, associated with excessive weight-gain (Tab. V), but differences are not significant.

The results have been summed up in a diagram (Fig. 2), which shows the principal factors of risk of shortened length of gestation, and of intrauterine growth retardation, at 32 weeks of gestation.

### Summary

The aim of this study is to prepare set rules for clinical decision making concerning the prevention of premature birth, i. e. selection of factors predicting high risk of prematurity. The goal is also to compare them with those children predicted to be dysmature.

This work is based on clinical records of prenatal consultations at the 32nd  $\pm$  2 weeks. We have compared frequency and distributions of 30 clinical signs (Tab. I, Fig. 1). The experimental groups include:

1. all mothers who gave birth to a child of less than 2500 g in 1969 at the obstetrical department of Port Royal.

**Keywords:** Mortality (perinatal), prematurity (etiology), prematurity (risk factors), prenatal care.

### Zusammenfassung

**Multifaktorielle Studie über das Frühgeburtsrisiko in der 32. Schwangerschaftswoche**

**I. Studie über die Häufigkeit von 30 prognostischen Kriterien**

In vorliegender Arbeit werden Richtlinien zur Verhütung unvorhergesehener Frühgeburten vorgeschlagen. Die Risikofaktoren, die zur Frühgeburt führen, wurden erforscht und dabei mit den Indizien verglichen, die es gestatten, Mangelgeburten vorherzusehen.

Wir werteten die Unterlagen der Schwangerschaftsuntersuchung in der 32.  $\pm$  2 Schwangerschaftswoche aus. Wir untersuchten die Häufigkeit und Verteilung 30 klinischer Symptome (Tab. I, Fig. 1). Dabei wurden zwei Gruppen einander gegenübergestellt. Die eine setzte sich aus all den Müttern zusammen, die ein Kind mit einem Gewicht unter 2500 g in der Geburtsklinik von Port-Royal 1969 gebaren. Eine Vergleichsgruppe bildeten 222 zufällig ausgewählte Mütter, deren Kinder im gleichen Jahr und in der

**Schlüsselwörter:** Sterblichkeit (perinatal), Frühgeburt (Ätiologie), Frühgeburt (Risikofaktoren), Schwangerschaftsfürsorge.

### 5. Conclusion

The results show that among all the 30 recorded characteristics, some are less favorable than others, either for a shortened length of gestation or for a low birth-weight, so that a predictive function for the risk of prematurity is best obtained by considering the whole set of characteristics.

In addition, the analysis indicates how the characteristics can be grouped into factors associated with a mechanism related to prematurity or to fetal growth retardation.

2. A control group of 222 mothers selected at random who gave birth to a child of more than 2500 g during the same year at the same hospital.

After separating two groups according to the length of gestation and birth-weight, we studied the frequency of the abnormal characteristics in the different groups.

We have shown each group of newborns has a special frequency curve (Fig. 2, Tabs. II—VI), with the higher frequencies and more numerous signs of abnormality in the group of the highest rate of prematurity.

We show that this curve is very different for mothers of dysmatures (small for dates) even if some of the clinical manifestations remain the same.

gleichen Klinik mit einem Gewicht über 2500 g geboren wurden.

Wir teilten die Gruppen nach Dauer der Schwangerschaft und nach Geburtsgewicht ein und erforschten die Häufigkeit von Krankheitszeichen in diesen Gruppen.

Wir konnten zeigen, daß jede dieser Gruppen durch ein spezifisches Diagramm bezüglich der Häufigkeit von pathologischen Symptomen charakterisiert ist und daß die Frequenz von Anomalien und die Anzahl von Krankheitszeichen um so größer sind, je ernsthafter die Frühgeburt ist (Fig. 2, Tab. II—VI).

Wir konnten darlegen, daß die Diagramme über die Häufigkeit bei den Müttern von Mangelgeburten differieren, wenngleich auch gewisse klinische Risikofaktoren die gleichen sind. Die Auswertung der Unterlagen dieser Gruppen beweist den Nutzen einer multifaktoriellen Analyse.

## Résumé

### Etude multifactorielle sur le risque de prématurité dans la 32<sup>ème</sup> semaine de grossesse

#### I. Etude de la fréquence de 30 signes spécifiques ayant valeur de pronostic

Le but de cette étude est la préparation de règles de décision utilisables pour la prévention de la survenue prématurée de l'accouchement. C'est la recherche d'indicateurs de risque pour la prématurité. Le but est également de comparer ces indicateurs à ceux qui permettent de prévoir la survenue d'enfants dysmatures.

Ce travail repose sur l'étude de dossiers établis à la consultation prénatale à 32 semaines  $\pm$  2 de grossesse. Nous étudions la fréquence et les distributions de 30 signes cliniques (Tab. I, Fig. 1). Les groupes comparés sont:

— d'une part, toutes les mères ayant eu un enfant de moins de 2500 g dans l'année 1969 à la Maternité de Port-Royal

— d'autre part, un groupe témoin de 222 mères choisies au hasard parmi les mères ayant eu un enfant de plus de 2500 g à la même maternité, la même année.

Nous avons séparé les groupes selon la durée de grossesse et le poids de naissance et avons étudié les fréquences des signes anormaux dans ces groupes.

Nous montrons que chacun de ces groupes peut être caractérisé par un diagramme spécifique des fréquences des signes anormaux, et que les fréquences des anomalies et le nombre des signes anormaux augmentent avec la gravité de la prématurité (Fig. 2, Tab. II—VI).

Nous montrons que les diagrammes de fréquence sont très différents chez les mères des dysmatures, même si certains signes cliniques de risque sont les mêmes. Cette analyse des groupes nous montre l'intérêt d'une analyse multifactorielle dans l'article suivant.

**Mots-clés:** Mortalité (périnatale), prématurité (étiologie), prématurité (facteurs de risque), soins prénataux.

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Prof. Dr. E. Papiernik-Berkhauer  
Service de gynécologie-Obstétrique —  
Hôpital Antoine Béchère  
157, Rue de la Porte de Trivaux  
F-92 140 Clamart/France