

Are vital Twins prematures? *

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The use of twins as a method in Human Genetics is based on an implicit assumption: that twin individuals are equivalent to single-born individuals and are therefore fully comparable to the latter.

This principle has one exception, which hardly affects its validity. The exception concerns several circumstances connected with antenatal life, whereby twins may differ from single-born babies and even from each other according to whether they are mono- or dizygotic. In both zygosity groups twins often differ from single-born individuals for their lower measurements at birth.

The twins' reduced weight and length at birth often result in their resemblance to prematures; this apparent equivalence has brought many Authors to lump twins and prematures together, rather than to consider them as two separate groups of newborn individuals with congenital debility.

The above considerations explain our request to be allowed to deal in this Symposium (devoted in part to the premature newborn) with the subject of newborn twins as *premature-like* individuals.

A visit to the Institute where you are today our welcome guests will reveal to you the size of our records of twin cases, already exceeding 9,000 pairs. Aided by a grant from the Italian National Research Council, we are transferring our records onto punch cards, and our IBM laboratory can already carry out large-scale investigations on our records.

Our report today concerns 2,440 living Italian twin pairs, born in the various regions and in different years, the average year of their birth being 1950.

Since zygosity is not sufficiently established in several cases, we have adopted Karn's criterion (1) by dividing our material only according to the sex composition of the pairs; we have added the further distinction of dividing unlike-sexed pairs ac-

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ording to the sex of the first-born. Our material was thus distributed into four classes as follows:

	First-born	Second-born	
All-male pairs	♂	♂	= 932
All-female pairs	♀	♀	= 817
Unlike-sexed pairs	♂	♀	= 357
Unlike-sexed pairs	♀	♂	= 334
			2,440

Our first analysis concerned the length of gestation. The level of information in our material was very high, since the length of gestation had been recorded in 2,316 out of 2,440 cases.

Recording the length of gestation in days and plotting the curve in 20-day classes on the ascissas and the resulting frequencies on the ordinates, we obtained the curve representing the frequency distribution as to length of gestation of twin pregnancies (Fig. 1). This curve, represented by the dotted line, is compared to the curve representing the equivalent distribution of single births (continuous line) based on the figures of the Italian Statistical Institute for 1958 (2).

A comparison of the mean values indicates a 12-day difference between twin and single pregnancies, the mean for the former being found at 258 days and for the latter at 270 days.

An analysis of the relationship between length of gestation and birth order in our material (Table 1) indicated a slight gradual increase in the length of gestation for

Tab. 1. Length of gestation (days)

Birth order	181-200	201-220	221-240	241-260	261-280	281-300	Total
1	1	26	76	131	317	13	564
2	1	21	47	112	295	8	484
3	—	7	29	58	163	6	263
4	1	6	15	33	110	3	168
5	1	4	1	16	49	1	72
6	—	1	3	8	30	—	42
7	—	—	—	7	18	—	25
8	—	—	1	1	10	1	13
over 8	—	—	2	1	12	—	15
Total	4	65	174	367	1004	32	1646

higher birth orders. While the average length of gestation for the first pregnancy is 257 days, in fact, increased birth orders correspond to longer gestation, reaching 267 days for the eighth pregnancy.

Let us consider now those traits that make twins premature-like, i. e. weight and

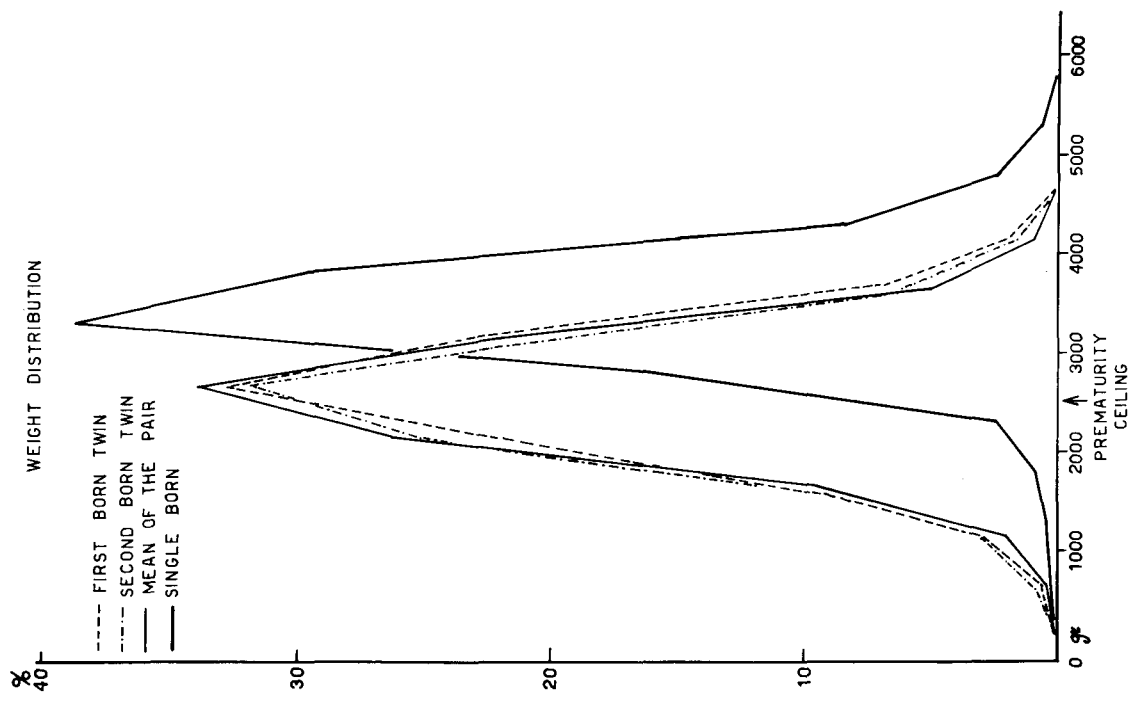


Fig. 2

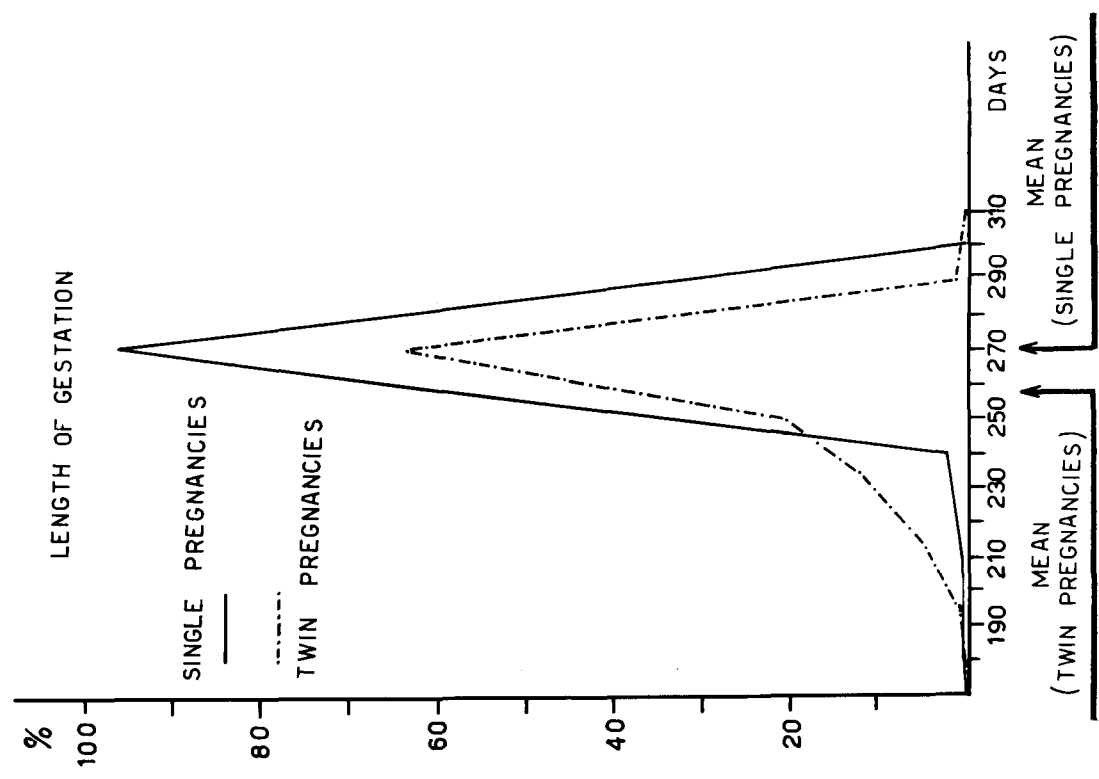


Fig. 1

length at birth. Information concerning weight at birth is recorded in most of our cases (99.37% of our material), while length at birth was found to be known in 23.52% of our cases only.

In our analysis of weight we have considered separately the weight distributions of the first-born, the second-born and the half-sum of the total maternal load deriving from the double product of conception.

Fig. 2 shows the frequency curves of weight for the first-born, for the second-born, for the half-sum of the pair and for single-born individuals (the latter derived from the data of the Italian Statistical Institute, 1958).

It is well known that cotwins may reveal substantial intrapair weight differences at birth (more pronounced for MZ pairs) (3), possibly resulting in blighting of one fetus; yet such differences are not expressed by our data, since they tend to an even distribution among the first-born and the second-born, thus being canceled also in the sum and half-sum of their weights. Besides, blighted fetuses and other cases leading to the death of one twin are not recorded here, since our material, as already stated, concerns only pairs with both twins still living.

In any case we can state that the means and variances concerning the first-born, the second-born and the half-sum of their weights are concordant, giving $2,650 \pm 614$ grams as the mean value for the weights of vital newborn twins. (The mean weight for the single-born, according to Anderson, Brown and Lyon (4), based on white newborn babies in the U. S., is $3,500 \pm 600$ grams).

It should be noted that the mean birth weight for our twin material is barely above the upper limit of prematurity, which the WHO convention sets at 2,500 grams. Thus only less than half of vital twins, representing 8/9 of the minus-variants in our Gaussian curve, may be considered as premature according to their birth weight. Less than half, or rather less than 40%, and this represents another relevant finding.

Among the single-born, instead, only a small fraction of the minus-variants for birth weight do not reach the threshold of maturity, fitting well enough the 12% of premature listed by Italian vital statistics.

The higher mode of birth weight for the single-born and the lower mode for twins indicate, in our case, a limited dispersal of values for the former and a wider dispersal for the latter.

In Fig. 3 the frequency curve of birth weights for the single-born is compared to the curve of total birth weights of our twin pairs (representing the actual maternal load). Dispersal is considerably higher in the case of twin pregnancies, the means and variances being $3,350 \pm 600$ and $5,293 \pm 1,159$ grams respectively.

The striking increase of the total maternal load in twin pregnancies as compared to that of single pregnancies seems to be out of proportion to the average difference of only ten days of gestation between the two groups. This is further emphasized by the fact that twins, each contributing individual movements, add a higher dynamic load to the increased static load. We are thus led to believe that the greater dynamic and static stresses induced by a twin pregnancy may be only contributing rather than principal factors in the induction of labor. This may support the hypothesis that the crit-

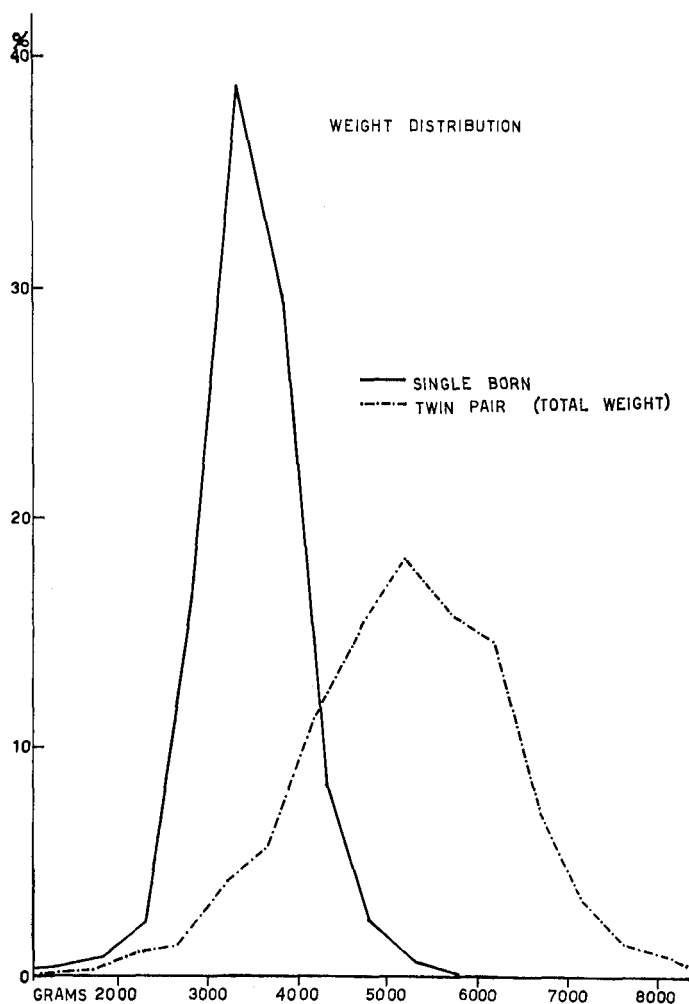


Fig. 3

ical discharge of oxytocin, responsible for the induction of labor, would depend on a mechanism other than a simple uterine stimulus reflex. (5).

A further analysis of the total birth weight of twin pairs revealed the following mean values for the different sex combinations:

All-male pairs	5,313 ± 1,115 grams
All-female pairs	5,074 ± 1,128 grams
Unlike-sexed pairs	5,293 ± 1,159 grams

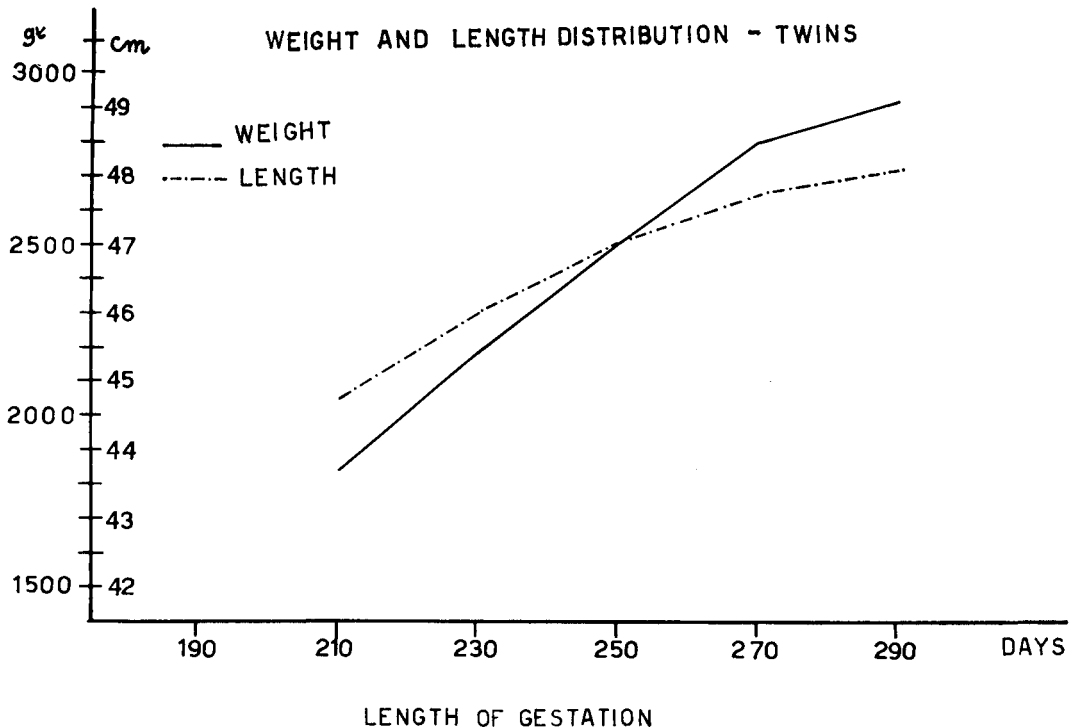


Fig. 4

The significance of the difference between all-male and all-female pairs is far in excess of the 0,001 level, thus indicating that they tend to duplicate the relationship between male and female single-born babies.

The weight ratio between all-male and all-female pairs is not reflected in the unlike-sexed pairs, since the latter reveal a mean weight exceeding the expectation based on the presence of one female twin: unlike-sexed pairs tend to behave like all-male pairs in this respect. This significant finding¹ concerning dizygotic unlike-sexed twin pairs seems to result from intra-pair influences.

Fig. 4 shows the curves for length and weight at birth in our material as related to the different classes of length of gestation. The two curves representing length and weight are quite similar, and their slight difference seems to reflect the known different patterns of development of these two traits in the auxologic period.

The mean value of length at birth for twins in our sample is 47.1 ± 6.9 cm.

¹ The comparison between the means for all-male and for all-female pairs gives a value of $T = 4.27$ with $p = 3/100,000$ — The comparison between the means for unlike-sexed pairs and for all-female pairs gives a value of $T = 3.25$ with $p = 16/100,000$, while the comparison between the means for all-male and for unlike-sexed pairs gives a value of $T = 0.33$ with $p = 36,317/100,000$.

These analyses make it possible to reach some preliminary conclusions.

Let us consider in the first place the definition of the International Classification of Diseases (6) according to which a premature is a newborn weighing 2,500 grams or less or, if the weight is unknown, born from a pregnancy lasting less than 37 weeks. This definition introduces two separate criteria, i. e. weight at birth and length of gestation, considering their limit values, or ceilings, below which we locate the area of immaturity.

Let us now discuss our mean values for twins compared with the ceiling values for prematurity as represented in Fig. 5.

The column of dotted-line histograms represents the ceilings for prematurity as defined by the International Classification of Diseases for weight and length of gestation and by Ylppö (7) for length. The full-line histograms represent our data for twins and, for the newborn, the data from the Italian Statistical Institute as to length of

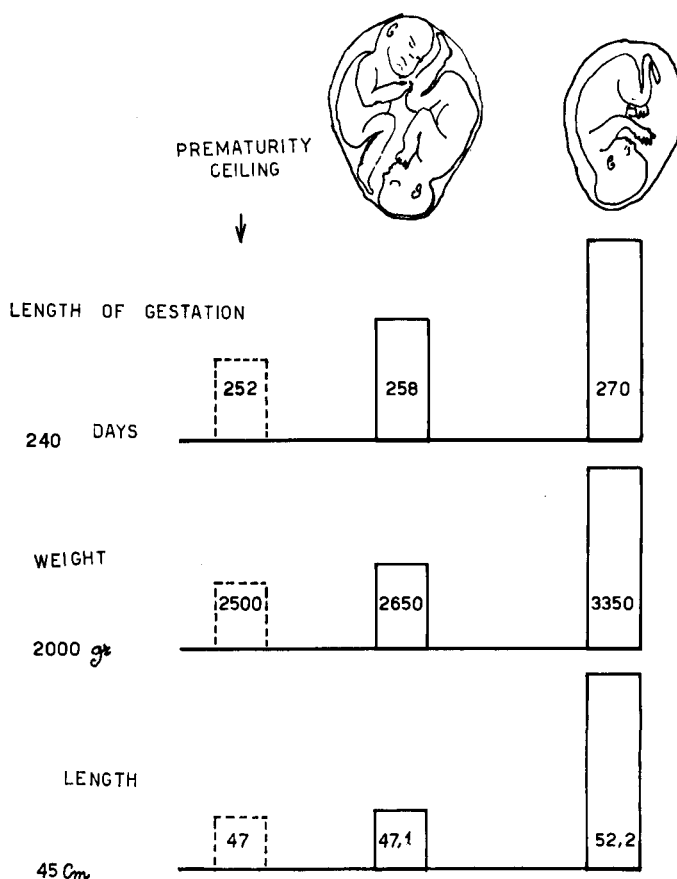


Fig. 5

gestation and for birth weight, and from Föllmer and Könninger (8) as to length at birth.

Concerning the length of gestation, if the ceiling for prematurity is set at 37 weeks, this means a maximum of 252 days, i. e. below the mean value of 258 days obtained by us for the length of gestation in twin pregnancies. As a consequence, considering a gaussian distribution, only less than half of vital twins could have been classified as premature from this obstetrical point of view.

Concerning birth weight, we find that the mean value of vital twins exceeds by 150 grams the ceiling adopted to discriminate prematures. Here again the gaussian distribution indicates that more than half of all vital twins could not be included in the group of prematures.

As for length at birth, not mentioned by the International Classification, we refer to Yllpö's criterion according to which the length of the premature at birth varies between 31 and 47 cm. Accepting this value and considering that the mean value for length in our twin sample is 47.1 cm., we reach again the same conclusion, that at least one half of all twins, using length at birth as a criterion, cannot be considered as prematures.

It is quite obvious therefore that to consider twins in general as prematures is wrong in at least 50% of all cases both obstetrically (length of gestation) and anthropometrically (weight and length at birth).

As for those twins who do remain within the limits of prematurity, we must note that the meaning of their minus-variance is quite different from that of the single newborn.

We know that, within 12 months after their birth, twins easily reach the weight and size values of the newborn, from which they cannot later be distinguished (9). Their limited growth during pregnancy seems to be due less to reasons of fetal sufferance than to auxologic limitations (ascribable in part perhaps to the physical limitations due to the presence of the other fetus in utero, in part to limitations in the maternal supply, or some other such reason). In most cases the reasons for twin minus-variance in prenatal growth seem to remain within the limits of the adaptation of the phenotype to extrinsic conditions, i. e. within physiologic variability.

In the single newborn the causes of spontaneous prematurity must be related instead to genetic or embryopathic intrinsic factors, specifically significant *quoad valetudinem*.

On the basis of the above considerations we are in full agreement with Gundborg Uddenberg (10) who, in his analysis of newborn individuals weighing under 2,500 grams, excluded twins with the following statement: « No twins were accepted for this investigation. The reason for this exclusion was that it is less certain whether it is justified to class twins as premature solely because of low birthweight ».

In conclusion we feel we can state that either twins are not premature because their measurements do not fall within the limits accepted for prematurity, or else they differ from the majority of single-born prematures because their immaturity is due to extrinsic conditions.

In the latter case they should be considered *auxologically* as potentially mature and *practically* as "premature-like".

Summary

The Authors have analyzed the data concerning length of gestation and neonatal weight and length measurements in 2,440 living twin pairs (from the files of the Mendel Institute), in order to verify the frequent assumption that all twins should be considered as prematures and, as such, affected by congenital debility.

Comparing their findings with the standard values for prematures, they reach the conclusion that the majority of twins who have survived the perinatal period were not prematures. Furthermore, the less developed among such twins differ from single-born prematures by reason of their subsequent normal auxologic development, whereby the Authors propose that they should rather be considered as "premature-like".

Literature

1. KARN MARY N.: *Annals of Eugenics*, Vol. 16, Part 4, 365-377, 1952.
2. *Annuario ISTAT* (1958).
3. GEDDA L., POGGI D.: *A. Ge. Me. Ge.*, XIII, 1. (1964).
4. ANDERSON N. A., BROWN E. W., LYON R. A.: *Amer. J. Dis. Childr.*, 65, 523, 1943.
5. KOWLESSAR M.: *Physiology of prematurity*, Josiah Macy Jr. Foundation, 1961.
6. *International Classification of Diseases*, 1948.
7. YLPPÖ A.: *Z. Kinderheilk.*, 24, 111, 1919.
8. FÖLLMER and KÖNNINGER: *Arch. Gynäk.*, 179, 694-708, 1951.
9. BRAUNS L.: *Ztschr. f. Kinderforsch.*, 43, 2. 86-129, 1934.
10. UDDENBERG GUNDBORG, Ejnar Munksgaard: Copenhagen, 1955.
11. BROCK J.: *Biologische Daten für den Kinderarzt*, Springer-Verlag, 1954.
12. JABAT K.: *Ann. Hum. Genet.*, 1964 27, 261.
13. GEDDA L.: *Twins in history and science*, Charles C Thomas, Springfield, 1962.

RIASSUNTO

Gli Autori hanno analizzato i dati relativi alla durata della gravidanza ed allo sviluppo pondero-staturale neonatale in 2440 coppie di gemelli viventi (tratte dalla cartoteca dell'Istituto G. Mendel) per verificare la comune asserzione che i gemelli debbano essere considerati affetti da debilità congenita perchè prematuri. Un raffronto dei dati così ricavati con i valori standard entro cui si collocano i prematuri conduce alla conclusione che i gemelli che abbiano superato il periodo perinatale sono prevalentemente nati maturi. D'altra parte i meno sviluppati si differenziano dai prematuri mononati per il loro successivo sviluppo auxologico normale che suggerisce di classificarli piuttosto come « prematurosimili ».

RÉSUMÉ

Les Auteurs ont analysé les données relatives à la durée de la grossesse et au développement pondéro-statural néonatal chez 2440 couples de jumeaux vivants (tirés de la cartothèque de l'Institut Mendel) dans le but de vérifier l'affirmation courante d'après laquelle les jumeaux devraient être considérés atteints de débilité congénitale, en tant que prématurés. Une comparaison des données ainsi obtenues avec les valeurs standard dans lesquelles les prématurés trouvent place, conduit à la conclusion que les jumeaux ayant dépassé la période périnatale sont presque toujours nés à terme. D'autre part, les moins développés se distinguent des non-jumeaux prématurés en raison de leur successif développement auxologique normal qui suggère de les classifier plutôt comme « prématuré-semblables ».

ZUSAMMENFASSUNG

Verf. untersuchten die Daten bezüglich der Schwangerschaftsdauer und dem geburtlichen Gewichts- und Grössenwachstum von 2440 lebenden Zwillingen (aus der Kartothek des G. Mendel-Institutes, Rom), um zu sehen, ob Zwillinge, wie allgemein behauptet wird, Frühgeburten und demzufolge mit angeborener Schwäche behaftet sind. Ein Vergleich der auf diese Weise gewonnenen Daten mit den Standardwerten für Frühgeburten führte zu dem Schluss, dass Zwillinge, welche die perinatale Periode überwunden haben, vorwiegend ausgereift zur Welt kommen. Die weniger entwickelten Kinder unterscheiden sich andererseits von den frühgeborenen Einzelgeburten durch ihre später normale Wachstumsentwicklung, weshalb man sie vielleicht als « frühgeburtähnlich » bezeichnen könnte.