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Normal chromosomes in liveborn neonates weighing less than 1000 g

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Cytogenetic investigations were performed in 37 phenotypically normal, liveborn immature neonates. Their mean birth weight was 758 g (range, 490–980 g), the mean gestational age was 24.2 weeks (range, 20–28 weeks). All the infants had normal karyotypes, no conspicuous structural aberrations and variants were found. It is presumed that while pregnancies with chromosomally abnormal zygotes are often terminated as fetal wastage or stillbirth, the phenotypically normal liveborn babies born even at a very early gestational age are likely to have normal chromosomes.

Several studies have shown that about 50% of first trimester abortions are associated with chromosome aberrations. The frequency of cytogenetic abnormalities sharply declines by advancing gestational age [3], however, as compared with normal unselected neonates, some surveys suggest a 3 to 4-fold incidence of chromosome abnormalities in premature infants [1, 4, 5]. This could not be confirmed by Bregman et al. [2], morover the materials of these studies had three essential limitations:

1. They were rather heterogeneous, involving both malformed and apparently healthy newborns.

2. Prematurity was diagnosed partly on the basis of clinical signs, partly considering the birth weight being under 2500 g.

3. The chromosome examinations were done mainly with traditional, non-banding procedures.

Thus, it can still not be judged whether prematurity or rather immaturity in itself is associated with an increased incidence of major or minor cytogenetic defects. The purpose of this study was to investigate by banding methods the karyotypes of apparently normal very low birth weight liveborn neonates.

Material and Methods

In our referral neonatal unit a total of 43 neonates whose birth weight was less than 1000 g, were karyotyped. Their gestational age was calculated from the mother's last normal menstruation. Two of them had major birth defects: anencephaly

This work is dedicated to Professor Julius Mestyán on the occasion of his 60th birthday.

and congenital heart malformation. Although their karyotype proved to be normal, they were excluded from the study. In four other cases no satisfactory preparations were obtained, thus we report here the results of 37 morphologically normal live-born immature neonates. The majority of these babies died in the perinatal period, at autopsy no inner malformations were found in any of them.

For cytogenetic investigations peripheral blood was taken on the 1st to 4th day of life. The whole blood lymphocyte cultures were harvested after 70 hours, 0.075 mol/l KCl solution was used for hypotonic shock. The air-dried preparations were routinely stained with traditional Giemsa and with a trypsin-Giemsa G-banding method. Twenty mitoses were microscopically examined and at least 3 conventionally stained and 3 G-banded cells were photographed. If there was a suspicion of structural aberration, additional slides were analysed with C and Q-banding techniques. The length of the Y-chromosome was measured in all boys in at least 5 conventionally stained mitoses, and expressed as $Y/F_{(mean)}$ ratio. A "long Y" variation was diagnosed when the Y/F ratio was greater than 1.00.

Results and Discussion

As shown in Table I, the karyotype was normal in every examined infant. The modal chromosome number was 46 in each case, the rate of hyper- and hypodiploid artifacts was less than 4% which corresponds to the standards in our laboratory.

Out of structural aberrations, translocations, ring chromosomes, exchange figures, inversions and insertions were not observed. Lacking an adequate control group, the number of chromatid and chromosome breaks and gaps, and of satellite associations was not evaluated, but their occurrence did not seem to exceed the usual level. Having had only a small number of late metaphase cells the exact sequence of centromere divisions could not be determined, yet, chromosomes No. 18 and 2 appeared to be the first, and the acrocentrics the last to separate. This pattern corresponded to that obtained previously in healthy control children and adults in different laboratories [6, 7, 11].

As regards to so-called normal variants, no conspicuous phenomena were seen among the autosomes. In one boy a "long Y" with a Y/F ratio of 1.10 was found. Because of the small number of observations, the 1/19, i.e. 5.2% frequency permits no statistical analysis and conclusion, but a significant difference from the Y-variant frequency of consecutive newborns seems rather unlikely. The mean $\pm$S.D. values of the Y/F ratios of all boys proved to be 0.89 ± 0.09 including the single long Y, and 0.88 ± 0.08 excluding it. These did not differ significantly from our normal value of 0.90 ± 0.09, previously determined in 20 healthy medical students.

Patil and Lubs [9] and Nielsen [8] described an association of long Y chromosomes with fetal loss. The present results did not confirm a correlation between long Y's and premature termination of pregnancy, however, further studies are needed to clarify the effect of the length of the Y chromosome on pregnancy in humans.

TABLE I

The applied cytogenetic methods and the karyotypes of the prematures examined

No.	Birth weight, g	Gestational age, week	Fate of neonate	Cytogenetic method	Karyotype
Girls					
1	500	?	died	T, G	46, XX
2	550	21	died	G, C	46, XX
3	600	23	died	T, G	46, XX
4	640	22	died	T, G	46, XX
5	650	22	died	T, G	46, XX
6	690	24	survived	T, G, C	46, XX
7	710	23	died	G	46, XX
8	750	24	died	T, G	46, XX
9	750	26	died	T, G	46, XX
10	800	24	survived	G	46, XX
11	800	?	died	T, G	46, XX
12	850	25	died	T, G	46, XX
13	850	24	died	T, G	46, XX
14	900	?	died	T, G	46, XX
15	900	26	survived	T, G	46, XX
16	900	25	died	T, G	46, XX
17	900	26	died	T, G	46, XX
18	910	28	died	T, G	46, XX
Boys					
19	490	?	died	T, G	46, XY
20	550	20	died	T, G	46, XY
21	590	21	died	T, G	46, XY
22	620	22	died	T, G, C	46, XY
23	650	?	died	T, G, Q	46, XY
24	700	24	died	T, G	46, XY
25	700	25	died	T, G	46, XY
26	700	?	died	T, G	46, XY
27	750	23	died	T, G, C	46, XY
28	800	25	died	T, G, Q	46, XYq+
29	800	25	survived	T, G, C	46, XY
30	800	24	died	T, G	46, XY
31	800	26	died	T, G	46, XY
32	830	25	survived	T, G, Q	46, XY
33	900	?	died	T, G	46, XY
34	900	25	died	T, G	46, XY
35	900	26	survived	T, G, C	46, XY
36	950	26	died	T, G	46, XY
37	980	28	survived	T, G, Q	46, XY

T = traditional (non-banding) Giemsa staining, G = trypsin-Giemsa G-banding, C = C-banding, Q = fluorescent Q-banding.

In conclusion, no chromosome abnormalities or conspicuous variability were found in a group of very low birth weight infants. The absence of major chromosome aberrations in our 37 patients excludes frequencies of more than 8% at the 95% confidence limit. According to gestational age these liveborn neonates were quite close to late midtrimester abortuses in whom significantly more chromosome abnormalities and structural varia-

tions have often been described. One may conclude that pregnancies bearing chromosomally abnormal zygotes develop abnormally and are terminated as fetal wastage or stillbirth, while the premature births of immature liveborns with normal phenotype are due to causes other than cytogenetic. This is in accordance with the late but still valid thesis of Ruzicska and Czeizel [10] that liveborn neonates represent a highly selected population.

From the practical point of view our findings suggest that in apparently normal liveborn neonates the very low birth weight in itself is no indication for routine cytogenetic investigations.

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