

Natural History of Trisomy 18 and Trisomy 13: II. Psychomotor Development

Bonnie J. Baty, Lynn B. Jorde, Brent L. Blackburn, and John C. Carey

Division of Medical Genetics, Department of Pediatrics (B.J.B., B.L.B., J.C.C.), and Department of Human Genetics (L.B.J.), University of Utah School of Medicine, Salt Lake City, Utah

Developmental data were abstracted from medical records on 50 trisomy 18 individuals ranging in age from 1 to 232 months and 12 trisomy 13 individuals ranging in age from 1 to 130 months. Data on the age when trisomy 18 and trisomy 13 children achieved developmental skills were collected from a larger group of 62 trisomy 18 individuals and 14 trisomy 13 individuals whose families filled out parent questionnaires. Developmental quotient (DQ), defined as developmental age divided by chronological age, averaged 0.18 for trisomy 18 and 0.25 for trisomy 13. There was a dramatic drop in DQ from infancy to later childhood. The highest DQs and the greatest variation in DQs were in the first 2–3 years of life. Developmental ages in 7 skill areas were significantly different, with daily living and receptive language having the highest values and motor and communication skills having the lowest. When chronological age was taken into account, there was no significant difference in DQs in the same 7 skill areas, although there was a trend that was similar to the pattern of differences with developmental age. Older children could use a walker, understand words and phrases, use a few words and/or signs, crawl, follow simple commands, recognize and interact with others, and play independently. Walking and some toileting skills were also reported for trisomy 13. Although individuals with trisomy 18 and trisomy 13 were clearly functioning in the severe to profound developmentally handicapped range, they did achieve some psychomotor maturation and always continued to learn.

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INTRODUCTION

Little has been written regarding the developmental assessment of trisomy 18 and trisomy 13. Previous information comes mainly from individual case reports of older individuals. A few of these case reports include some detailed information about developmental progress [Gerhard, 1976; Smith et al., 1978; Smith et al., 1989] but most give sketchy information, if any. This is in large part due to the rarity of older individuals with full trisomies and the fact that any one practitioner is unlikely to see several older trisomy 18 or 13 children. The parent support group offered an opportunity to study a series of surviving individuals. One recent publication has reported on a series of older individuals, using the S.O.F.T. support group for identification of cases [Van Dyck and Allen, 1990].

METHODS

This study is part of a larger study of the natural history of trisomy 18 and trisomy 13. The initial part of the study involved sending questionnaires to families registered with the Support Organization for Trisomy 18, 13, and Related Disorders, which is known as S.O.F.T. A total of 98 trisomy 18 families and 32 trisomy 13 families with nonmosaic trisomy answered a 4-page questionnaire, which included questions about demographics, birth data, growth, neonatal hospitalization(s) and operations, immunizations, psychomotor development, birth defects, medical complications, cause of death, and family history of other chromosome disorders. Data concerning all aspects except development have been reported in a separate publication [Baty et al., 1994]. Cytogenetic confirmation was achieved for 97% of trisomy 18 individuals and 97% of trisomy 13 individuals. Ages at the time of the developmental assessment ranged from 1 to 232 months (19 years, 4 months) for trisomy 18 and 1 to 130 months (10 years, 10 months) for trisomy 13. There were 41 trisomy 18 individuals (42%) and 12 trisomy 13 individuals (38%) surviving to age 1 year. The developmental questions consisted of a list of

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Address reprint requests to Bonnie Jeanne Baty, Department of Pediatrics, University of Utah Medical Center, Salt Lake City, UT 84112.

developmental stages, and parents were asked the age or date at which their child had achieved those stages. A total of 62 trisomy 18 families and 14 trisomy 13 families provided information on psychomotor development.

The second part of the study involved obtaining medical records from the same families that filled out the parent questionnaires. The two groups did not completely overlap, because we could not obtain medical records on some individuals whose parents supplied developmental information, and we obtained medical records on some individuals whose parents did not supply developmental information. The subset of individuals with developmental records all had confirmation of full trisomy. If developmental testing had ever been done, records on the child's psychomotor development were requested. We obtained developmental records on 50 individuals with trisomy 18 and 12 individuals with trisomy 13. Of the individuals with developmental records, 29 with trisomy 18 and 8 with trisomy 13 were over the age of 1 year.

Data were abstracted from the developmental records and computerized using the Ingres database management program. Statistical analysis was performed using the BMDP package. The information abstracted included chronological ages, developmental ages for specific skill areas on specific developmental tests, individual skills recorded by the developmental specialists evaluating the child, feeding skills, and IQs. Many children were evaluated at multiple ages using multiple tests, while some children had very few entries. There were 28 different developmental tests used. The most common (the Bayley Scales of Infant Development, the Vineland Adaptive Behavior Scales, and the Alpern-Boll Developmental Profile) accounted for 44% of the measurements obtained.

Each individual developmental age (DA) entry was divided by the individual's chronological age (CA) at the time the DA was measured to obtain a developmental quotient (DQ) entry. This provided a measure of development that could be compared across different CAs.

RESULTS

The psychomotor development reported by parents is summarized in Table I. The table contains the mean, standard error of the mean, range, number of individuals reporting each stage, and the normal age range [Frankenburg et al., 1976; Moyers et al., 1974] for each skill.

As is often the case with conditions associated with mental retardation, the range of time in which a developmental level is achieved is wider than usual. Four of the trisomy 18 children and 1 trisomy 13 child were reported to use a few consistent signs. Five trisomy 18 children used a few consistent words. Many of the older children have a much more extensive receptive vocabulary. Five of the trisomy 18 children walked with a walker, and one trisomy 18 child and 2 trisomy 13 children cruised around furniture. No individual with trisomy 18 was reported to walk, but one trisomy 13 child walked at age 9. In addition to the child with trisomy 13 reported, two of the authors have personally met another 13 year old with trisomy 13 who walks.

The remainder of the data reported was abstracted by one of the authors (BJB) from the medical records. Table II shows the mean CA, mean DA, and mean DQ for various age groups, along with the standard error of the mean for each. The number of observations in each group and the number of children on which these observations were made are also reported. Figure 1 summarizes the data on DQ in graphic form. For both conditions, mean DQs drop dramatically with age (one-way analysis of variance; $P < 0.0001$). Overall, mean DQs were significantly higher for trisomy 13 than for trisomy 18 (one-way analysis of variance; $P < 0.0001$). These differences were most pronounced at ages 12–36 months and over 60 months.

Individual DQs plotted against CAs for trisomy 18 (Fig. 2a) and trisomy 13 (Fig. 2b) show highly similar patterns. A nonlinear regression analysis showed that a negative exponential curve provided the best fit to these

TABLE I. Developmental Achievements in Trisomy 18 and Trisomy 13

	Trisomy 18			Normal range	Trisomy 13		
	Av. mos. (SE)	Range	N		Av. mos. (SE)	Range	N
Smiled responsively	4.7 (0.5)	0.5–24	54	0–2	5.5 (1.3)	0.5–15	12
Held head up	9.0 (1.5)	0.3–36	33	0–2.5	9.5 (2.4)	0.7–24	10
Watched toy or face	4.4 (0.6)	0.2–24	57	0–1	8.4 (3.3)	0.9–40	12
Reached for object	9.6 (1.2)	2.5–36	38	3–5	14.2 (2.3)	4.5–30	10
Laughed out loud/giggled	13.0 (3.1)	2.3–96	36	1.5–3.3	10.4 (2.0)	4–20	9
Sat up with help	20.4 (2.9)	3.5–60	25	1.6–4.3	22.4 (3.1)	15–36	7
Sat up alone	38.5 (6.3)	7.5–72	12	4.8–7.8	31.0 (5.7)	23–42	3
Said consonant sounds	23.0 (6.2)	8.0–52	8	5.6–10	19.4 (7.6)	11.8–27	2
Rolled over	30.5 (16.5)	0.2–540	32	2.2–4.7	11.2 (1.9)	4–24	10
First tooth	11.5 (0.7)	4.0–20	30	4.0–17	10.0 (1.3)	4–18	10
Balanced on hands and knees	53.7 (18.1)	12–204	10	—	41.5 (6.5)	35–48	2
Walked in walker	39.5 (7.4)	24–60	5	—	32.5 (12.1)	9–58	4
Cruised furniture	72		1	7.4–12.7	56.5 (15.5)	41–72	2
Walked alone			0	11.2–14.4	112		1
Used signs	61.5 (9.9)	36–84	4	—	72		1
Number of signs	2 (0.4)	1–3	4		6		1
Number of words	3.4 (0.7)	1–5	5				0

TABLE II. Mean (\pm Standard Error) Chronological Ages, Developmental Ages, and Developmental Quotients for Trisomy 18 and Trisomy 13

Age (years)	Trisomy	Chron age (months)	Dev age (months)	DQ	Number of observations	Number of children
0-1	18	8.6 (\pm 0.6)	3.7 (\pm 0.5)	0.42 (\pm 0.04)	25	10
	13	6.6 (\pm 0.7)	3.3 (\pm 0.5)	0.48 (\pm 0.06)	11	3
1-3	18	25.2 (\pm 0.8)	3.9 (\pm 0.2)	0.17 (\pm 0.01)	76	15
	13	26.3 (\pm 0.9)	7.7 (\pm 0.4)	0.31 (\pm 0.02)	53	5
3-5	18	46.8 (\pm 1.2)	8.2 (\pm 0.8)	0.18 (\pm 0.02)	48	7
	13	44.1 (\pm 1.0)	7.3 (\pm 0.5)	0.17 (\pm 0.01)	26	5
>5	18	97.6 (\pm 4.4)	6.8 (\pm 0.4)	0.08 (\pm 0.01)	58	9
	13	92.7 (\pm 6.1)	13.3 (\pm 1.9)	0.13 (\pm 0.01)	25	2
All ages	18	48.5 (\pm 2.6)	5.7 (\pm 0.3)	0.18 (\pm 0.01)	207	26
	13	42.9 (\pm 3.0)	8.4 (\pm 0.5)	0.25 (\pm 0.01)	115	8

data. The highest individual DQs, as well as the greatest variation in DQs, clearly occur at the youngest ages. There are many individual measurements above 0.5. These higher DQs represent 6 different cases (4 have trisomy 18 and 2 have trisomy 13). Three of the children have only one measurement above 0.5, and 3 children have from 3 to 6 measurements above 0.5. The CAs of these high DQs range from 2 months to 50 months. They represent several different tests and skill areas. Thus, there seems to be no pattern of high DQ measurements, except that they are all at 50 months or below. The measurements above 100 months represent 1 trisomy 13 child and 3 trisomy 18 children. The values for the trisomy 13 child are higher than those of the trisomy 18 children, but the numbers are too small to permit generalization. In general, there is a sharp "drop-off" in DQ, representing an increasing distance from the developmental curve of average normal children, which would

ideally be a horizontal line at 1.0. The drop-off in the curve does not represent a loss of skills, but rather greater distance from the normal curve. It is clear from the information derived from parent reports and from these formal developmental assessments that these children generally continue to acquire new skills throughout their lives.

An average DQ at each CA for each child was also plotted to determine whether multiple measurements on the same child at the same age could bias the data. All three plots (for trisomy 18, trisomy 13 and combined data) looked essentially the same. Once again, trisomy 13 appeared to have somewhat higher scores in the older children.

Only two children had IQ scores recorded in their developmental records, both trisomy 18 children with IQ scores of 20. The children were ages 5 and 12. We did not find IQ scores useful, both because of the lack of data and

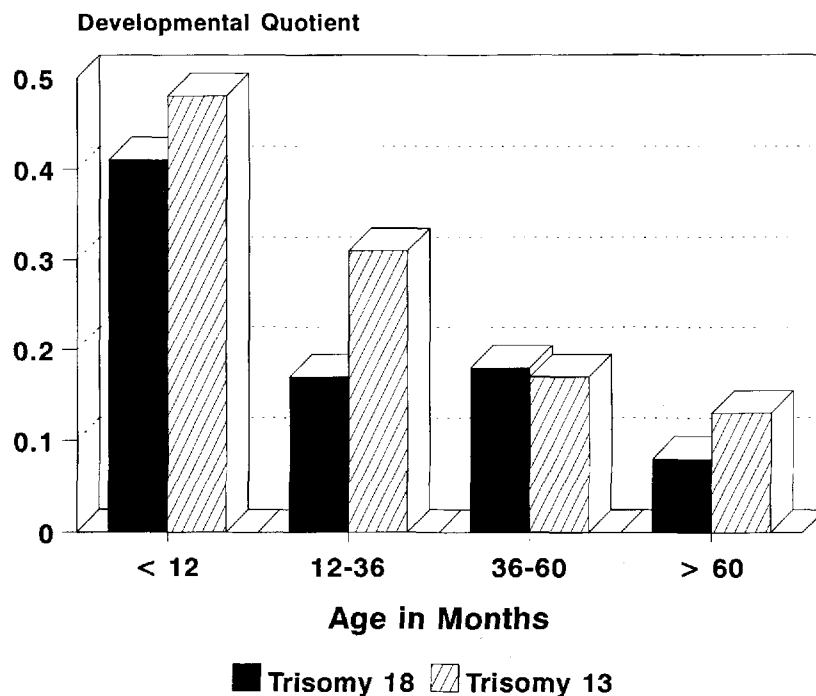


Fig. 1. Average developmental quotients at different ages in trisomy 18 and trisomy 13.

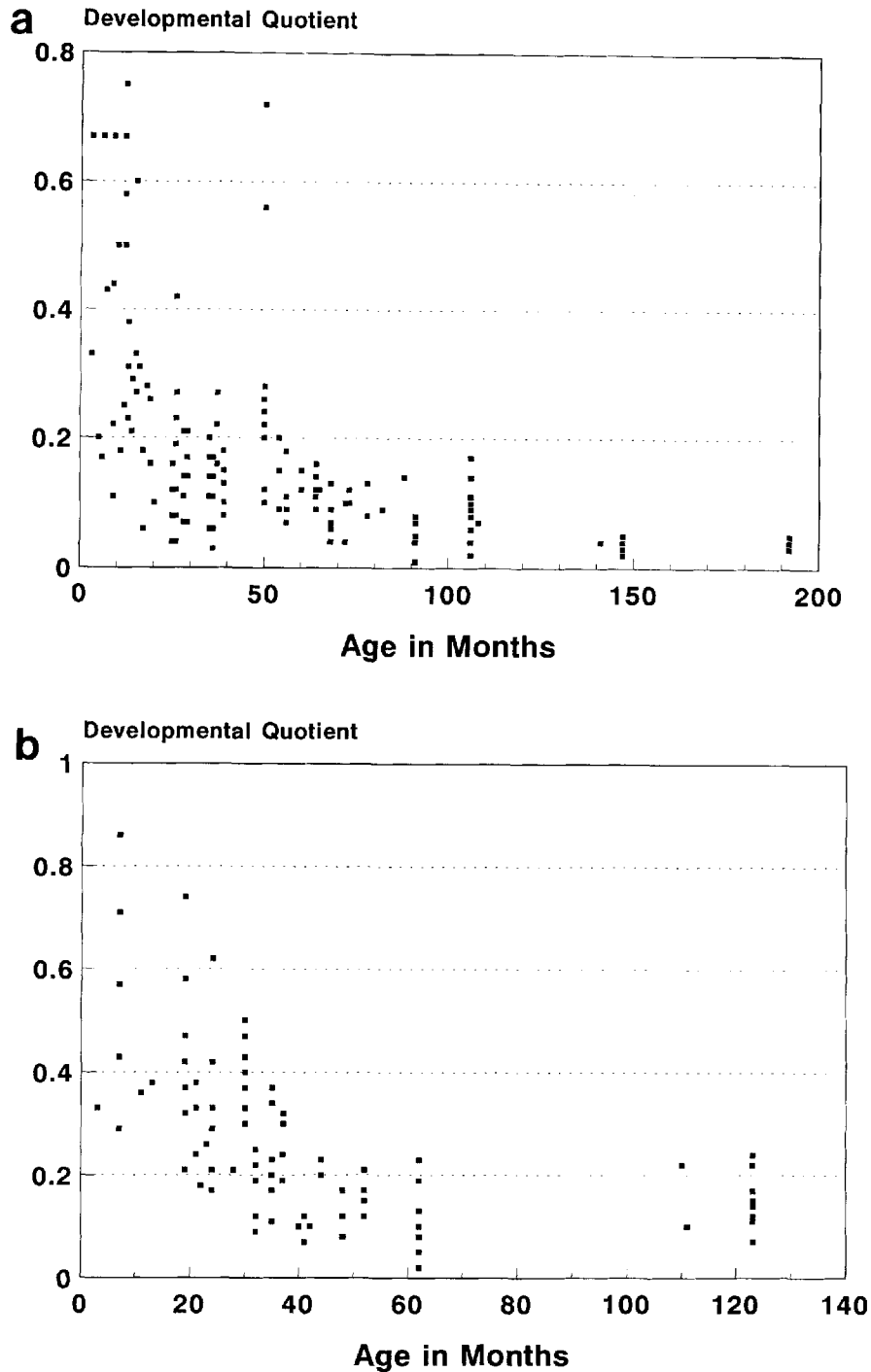


Fig. 2. (a) Developmental quotients (individual developmental age measurements divided by chronological age) by age in trisomy 18. (b) Developmental quotients (individual developmental age measurements divided by chronological age) by age in trisomy 13.

the relative lack of descriptive power of a single IQ score in the lower end of the IQ range.

Twenty-eight different developmental tests were used. The three most frequently used tests, the Bayley Scales of Infant Development, Vineland Adaptive Behavior Scales, and the Alpern-Boll Developmental Profile, accounted for 44% of the total tests. One-way analysis of variance

showed that these 3 tests gave significantly different mean values of both CA ($P < 0.0025$) and DA ($P < 0.021$). However, this is largely due to the fact that different tests tended to be given at different ages. DQ, in fact, did not differ significantly by test type (Table III). The other 23 developmental tests were performed on too few individuals to permit statistical analysis.

TABLE III. Developmental Assessment by Three Common Developmental Tests*

	Mean (\pm SE) CA (months)	Mean (\pm SE) DA (months)	Mean (\pm SE) DQ (months)
Bayley	40.0 (\pm 6.3)	5.0 (\pm 0.5)	0.19 (\pm 0.02)
Alpern	59.7 (\pm 8.0)	6.3 (\pm 0.7)	0.22 (\pm 0.05)
Vineland	75.3 (\pm 8.1)	6.9 (\pm 0.5)	0.13 (\pm 0.02)

* Some tests are combined. For example, a Bayley test may be given alone or in combination with any other developmental test, and it will be counted as an entry.

The data were divided into 7 main skill areas: receptive language, expressive language, communication, daily living, cognitive, social, and motor skills. There were no significant differences in mean CAs between the 7 skill areas. There were also no significant differences in CA between trisomy 18 and trisomy 13.

There were highly significant differences in DAs between many skill areas, using one-way analysis of variance ($P < 0.0001$). Table IV ranks the skill areas from highest to lowest DA. The highest DAs were for daily living, receptive language, and social skills, and the lowest DAs were for motor skills and communication. The differences remained statistically significant after applying a Bonferroni correction for multiple comparisons ($P < 0.05$). Daily living skills were significantly higher than cognitive ($P < 0.001$), motor ($P < 0.0001$), and communication skills ($P < 0.001$). Motor skills were significantly lower than social ($P < 0.001$), daily living ($P < 0.0001$), and receptive language skills ($P < 0.002$). Two-way analysis of variance of DA or DQ, using trisomy type and skill area as the treatment groups, showed that differences in skill areas did not vary according to the type of trisomy.

Table V shows the differences in mean DQs between skill areas, which should correct for the effect of CA on DA. There was a similar rank order of skill areas. However, the differences were no longer statistically significant by one-way analysis of variance ($P > 0.4$). This probably reflects the fact that the differences in DA are dependent on CA. Since the rank order of skill areas is similar for DA and DQ, it is possible that a larger number of subjects would have produced a significant difference in DQ. Since histograms of CA, DA, and DQ all revealed nonnormal distributions, nonparametric significance tests were also used, with the same results.

There were many specific skills commonly mentioned at different ages. For both trisomy 18 and trisomy 13,

the activities commonly documented in the first year were following, cooing, rolling, smiling responsively, reaching, and recognizing close adults. In the next 2 years, new activities included sitting supported, object permanence, imitation, playing baby games, sitting independently, and recognizing words. In the next 3 years (at ages 4–6) commando crawling, independent playing, following simple commands, helping with hygiene tasks, standing, understanding cause and effect, and use of signs were reported. The older children could identify common objects, use a walker, crawl, and understand words and phrases. Trisomy 13 individuals attained the same skills, and some also acquired some toileting skills and walking ability. The data on specific developmental skills which were collected from parents of these same children were very consistent with the data obtained from formal developmental evaluations.

We also abstracted information about feeding skills from the medical records. For trisomy 18, 33/50 (66%) documented gavage feeding, 54% as newborns. Breast feeding was documented in 4/50 (8%) and bottle feeding in 16/50 (32%). Several children were eating solid foods in the first year. Several children were being spoon fed or using a cup in the second year of life. A few individuals used a cup or finger fed independently. For trisomy 13, 4/12 (33%) documented gavage feeding, all as newborns, and 7/12 (58%) documented bottle feeding. Two children ate and drank with help at 30 and 54 months. Spoon feeding, use of a cup, and finger feeding were also documented.

DISCUSSION

This is a retrospective study which seeks to capitalize on an unusual data set. It has some attributes of a longitudinal study and some attributes of a cross-sectional study. Limitations include (1) an inconsistent data set with developmental data from many geographic locations, over different periods of time, with many types of tests and many examiners; and (2) the use of the term DQ, which is controversial among developmental specialists and should be thought of as a rough estimate of function. In spite of these limitations, we feel that this unique data set has considerable value in understanding the developmental progression of individuals with trisomy 18 and trisomy 13.

Our conclusions are:

1. There was a dramatic drop in DQ from infancy to later childhood in trisomy 18 and trisomy 13. The

TABLE IV. Mean Developmental Age (\pm Standard Error) in Months by Skill Area

All	Trisomy 18		Trisomy 13		
Daily living	9.6 (\pm 1.3)	Rec language	8.7 (\pm 2.4)	Social	11.1 (\pm 1.9)
Rec language	9.3 (\pm 1.6)	Daily living	8.3 (\pm 1.2)	Daily living	10.7 (\pm 2.3)
Social	8.4 (\pm 0.9)	Social	6.7 (\pm 0.7)	Rec language	10.3 (\pm 1.7)
Expr language	6.7 (\pm 0.8)	Expr language	6.0 (\pm 0.9)	Cognitive	7.7 (\pm 1.1)
Cognitive	5.7 (\pm 0.4)	Cognitive	5.1 (\pm 0.4)	Expr language	7.5 (\pm 1.4)
Motor	5.4 (\pm 0.4)	Communication	4.9 (\pm 0.5)	Motor	7.3 (\pm 0.7)
Communication	5.4 (\pm 0.4)	Motor	4.2 (\pm 0.3)	Communication	6.5 (\pm 0.8)

TABLE V. Mean Developmental Quotient (\pm Standard Error) by Skill Area

	All	Trisomy 18	Trisomy 13		
Rec language	0.24 (\pm 0.04)	Rec language	0.20 (\pm 0.05)	Cognitive	0.33 (\pm 0.06)
Daily living	0.23 (\pm 0.04)	Cognitive	0.19 (\pm 0.03)	Rec lang	0.31 (\pm 0.08)
Cognitive	0.22 (\pm 0.03)	Daily living	0.19 (\pm 0.05)	Daily living	0.26 (\pm 0.06)
Social	0.21 (\pm 0.02)	Social	0.18 (\pm 0.03)	Social	0.26 (\pm 0.04)
Expr language	0.19 (\pm 0.03)	Communication	0.15 (\pm 0.03)	Expr language	0.23 (\pm 0.06)
Communication	0.18 (\pm 0.03)	Expr language	0.14 (\pm 0.03)	Communication	0.23 (\pm 0.05)
Motor	0.18 (\pm 0.01)	Motor	0.14 (\pm 0.01)	Motor	0.23 (\pm 0.02)

data have a negative exponential distribution and are similar in both trisomy 18 and 13, although trisomy 13 had significantly higher DQs. The highest DQs and the greatest variation in DQs were in the first 2–3 years of life. The drop in DQ does not reflect a loss of skills, but instead reflects an increased lag in developmental progress compared to normal children.

2. Developmental ages in 7 skill areas were significantly different, with daily living and receptive language having the highest values and motor and communication skills having the lowest. When chronological age was taken into account, there was no significant difference in DQs in the same 7 skill areas, although there was a trend that was similar to the pattern of differences with developmental age.

3. Although individuals with trisomy 18 and 13 were clearly functioning in the severe to profound developmentally handicapped range, they did achieve many skills of childhood, and always continued to learn. Older children could use a walker, understand words and phrases, use a few words and/or signs, crawl, follow simple commands, recognize and interact with others, and play independently. Walking and some toileting skills were also reported for trisomy 13.

In the course of our contact with these families, it became clear that many parents resented the early message that their child would never interact with his or her environment and family. Many professionals conclude that a diagnosis of trisomy 18 or trisomy 13 means a hopeless outlook with survival in a vegetative state, or that the diagnosis is incompatible with life [Bos, 1992]. Many families with surviving trisomy 18 or trisomy 13 children think that the information they were given was more discouraging than necessary, and ignored the humanity of their child. It is important to parents that the

accomplishments of their children are acknowledged by the medical community. The range of DQ variation for different developmental skill areas is relatively small and may even seem inconsequential. However, a difference of several months of developmental skills in the first year of life has great meaning to families. It could mean the difference between a child who sits alone vs. a child who cannot sit unsupported, or the difference between nonresponsiveness vs. smiling, reaching out and recognizing close adults. It is important that families have this information when a diagnosis of trisomy 18 or trisomy 13 is made, either prenatally or postnatally.

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