

PROPORTIONALITY IN GENETIC SYNDROMOLOGY AND PERINATAL GROWTH ASSESSMENT

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Abstract: *Proportionality in genetic syndromology is a chronicle of the use of the Phantom, a single, unisex reference human to assess proportionality characteristics in sex chromosome aneuploidy and its use in assessing normal perinatal growth characteristics. Both applications were inspired by Otto Eiben and facilitated by interaction in symposia organized by him. Based on data assembled by Otto and his colleagues, a strategy was developed for assessing systematic effects associated with 47XYY, 47XXY, 47XXX, and 45XO aneuploidy. A comparison of 16 Turner's syndrome 45XO patients with 168 normal fertile 46XY controls showed the Turner's syndrome was associated with proportionally short proximal segmental lengths in both upper and lower extremities and suggests an error in estimating lower limb lengths from pelvic measures projected to the floor because of an atypical pelvis development. Based on discussion at Otto Eiben's first international symposium on Human Biology at Lake Balatonfüred in 1972, longitudinal perinatal growth characteristics assembled by Johanna Faulhaber on Mexican children, detected a three month proportional weight deflection point. This was confirmed in twenty five of twenty eight studies in the literature. This led to a three month deflection point hypothesis or a peak deflection point that occurs at the same gestational age in all children and that any prenatal insult (premature birth, malnutrition, very young mothers, alcohol, drugs or tobacco abuse) would not effect the peak but would be reflected in a slower decline in the slope to linearity thereafter to approximate adult proportionality values. A way to study the phenomena was suggested in an iconometry display of longitudinal data from the Saskatchewan Growth Study. The account and examples in this paper are just a few of hundred of studies and thousands applications facilitated or inspired by Otto Eiben, one of the greatest anthropologists of his generation and of all time. His kindness, generosity, scholarship and commitment to service to human kind will enrich and inspire generations to come.*

Keywords: *Sex chromosome; Aneuploidy; Anthropometry; Eiben; Faulhaber; Phantom; Proportionality; Perinatal growth; Three month deflection hypothesis.*

During the Cold War Years, Marcel Hebbelinck arranged several lecture tours for me to help link with colleagues in Eastern Europe. On one of these occasions I visited Budapest and met with Mihály Nemessuri and Péter Apor. I learned from them that Barbara Heath was in Budapest and staying at the Victoria Hotel. I immediately telephoned to say hello. Barbara who was returning from a visit to the USSR. She invited me to have breakfast with her the following day. She also invited Otto Eiben. This was the first time (in May 1975) we met, although we knew each other from the literature and I had a copy of his book: *The Physique of Women Athletes* (Eiben 1972).

Barbara was in rare form. She was laughing, had bold plans and was, as usual, very enthusiastic. I accused her of giving Otto Eiben a mesomorphy rating half a point higher

than he deserved, a bias because she liked him. "Maybe I should give him a whole point?" In Pau Pau, New Guinea where she conducted her epic genealogical histories she is known as the "Woman Who Laughs a Lot" (Stori Bilong Pere, Barbara Honeyman Roll 1982). At the end of our breakfast visit, she said how pleasant it was to meet with us but we were to go away for two days and that she didn't want to have anything more to do with us because Otto and I had things to talk about.

So it was. Otto and I discussed science, meaning and purpose. He showed me an elegant cardboard model, with sliding strips he made that served to quantify proportionality profiles based on a factorial analytic system he designed. I was awed. We then looked at the Phantom proportionality profiles on the same data I brought with me. We got perfect agreement on relevant variables.

Near the end of the two days, when we slept little, Otto said. "I will never use factorial analysis again, the Phantom shows the same thing. It is more comprehensive and elegant."

I was staggered at his response. He was absolutely detached from his model and beautiful calculation device. I protested. He smiled and said, wait and see. Then, he changed the discussion topic and had a look at data on Turner's syndrome and normative controls that he and his colleagues assembled and later reported (Eiben et al. 1974)

He also reported these data and some aspects of proportionality in sport and medical practice in Kinanthropometry II. Leuven, Belgium. Of particular interest, verifying the use of the Phantom, was in the assessment of systematic proportionality characteristics in patients with gonadal dysgenesis (Eiben et al. 1980).

At Simon Fraser University a course on Kinanthropometry had a problem solving component under guided learning by teaching assistants. The students reported their enterprises in a series of 43 Student Symposia during my tenure at the university. The formal presentations (many audio and some videotaped) were patterned on the international symposia organized by Otto Eiben, in particular the first of a series of seven in Human Biology Balatonfüred in 1976. One of the student papers was based on the data and initial discussions I had with Otto. The paper was rewritten by Roger Miller, his wife, A. Rapp and Machteld Roede (Miller et al. 1980).

When we projected data on patients with 47XYY, 47 XXY, 47XX and 45XO we showed the comparative size and proportionality characteristics illustrated in Figure 1.

Phantom z values or proportionality score are displayed in Figure 2 showing pronounced differences associated with each aneuploidy.

I still use the Figure 3 below didactically to show that the classical description of Turners' Syndrome is misleading. The "long arms and short legs" and other characteristics are ill defined. Both proximal segments in the upper and lower segments are proportionally short and atypical pelvic development in the Turner's Syndrome was a spurious indicator of lower extremity length. The truncation of proximal segmental length and normal female pelvic development should give us timing effect and influence of the aneuploidy.

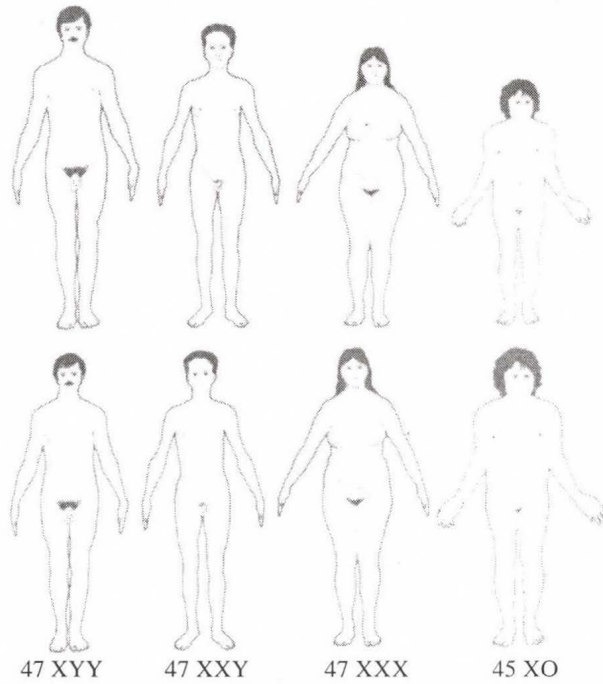


Figure 1: Upper row, size characteristics, lower row, proportionality characteristics when projected to the same stature and scaled geometrically.

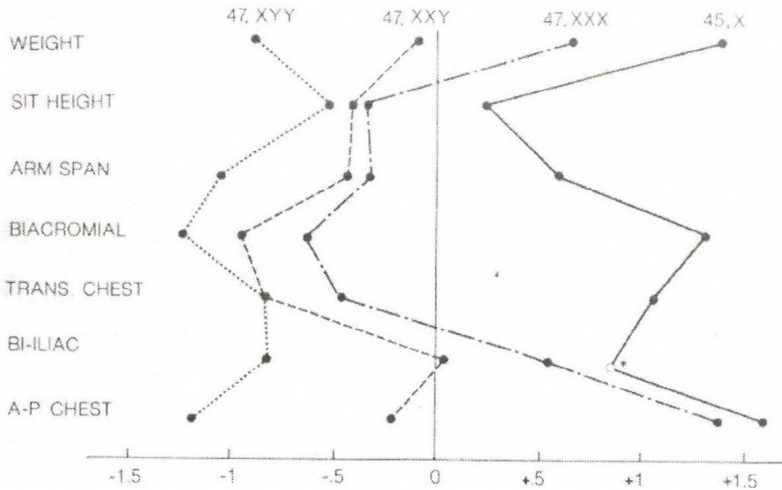
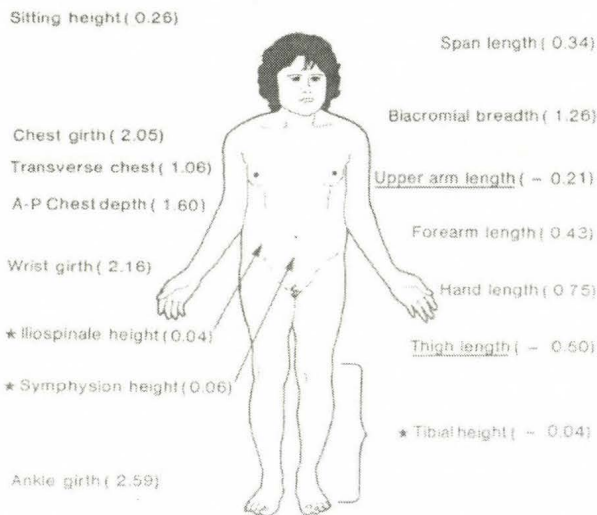


Figure 2: Proportional differences in Phantom z-values for left to right 47XYY, 47 XXY, 47XX and 45XO sex chromosome aneuploidy based on data by Eiben, Sándor and László (1974).

Phantom z-values

Differences 45,xo versus 46,xx controls



* indicates negligible differences. Underlined values are proportionally smaller all other values are proportionally larger

Figure 3: Pictorial representation of differences in z-values obtained by subtracting mean z-values of 16 Turner's patients for 169 female control subjects. Calculated from data assembled by Eiben and colleagues.

The 3 months proportionality deflection hypothesis

The Balatonfüred discussions that Otto and I had with Johanna Faulhaber, immediately set her to analyzing her longitudinal data reported in her *Investigacion Longitudinal del Crecimiento* (Faulhaber 1974) resulting in the first comprehensive proportionality assessment of longitudinal data (Faulhaber 1978).

The startling finding was a three month proportional body mass defection point at about 7.5 z. This became the basis for an Honors thesis by Gina Lau Pau (1980) who scoured the literature to determine if Johanna's finding was a common phenomenon or was unique to her Mexican study. Despite, the lack of background information, socio economic level at gestational age, and frequency of the measurement occasions, the phenomenon was noted in 25 of the 28 sets of data assembled. The three exemptions may not have had frequent enough measurement occasions. Perhaps weekly assessment is needed.

We made generalizations about genetic syndromology and perinatal events in two chapters in textbooks. Ross and Ward (1980) and Ross, Ward, Sigmon and Leahy (1980).

Subsequently, we proposed a new growth hypothesis in the inaugural Congress of the newly founded International Society for the Advancement of Kinanthropometry in Glasgow, Scotland. Ross and Ward (1986). (n.b. Otto Eiben was a elected as a charter executive member of the new society).

Richard Ward and I re-analyzed reports on perinatal events and proposed the *three month deflection point hypothesis* where a peak deflection point occurred at the same gestational age from conception in all children and that any prenatal insult (premature birth, malnutrition, very young mothers, alcohol, drugs or tobacco abuse) would not effect the peak but would be reflected in the slower decline in the slope to linearity thereafter to the adult 0.0 z as illustrated in Figures 4 and 5.

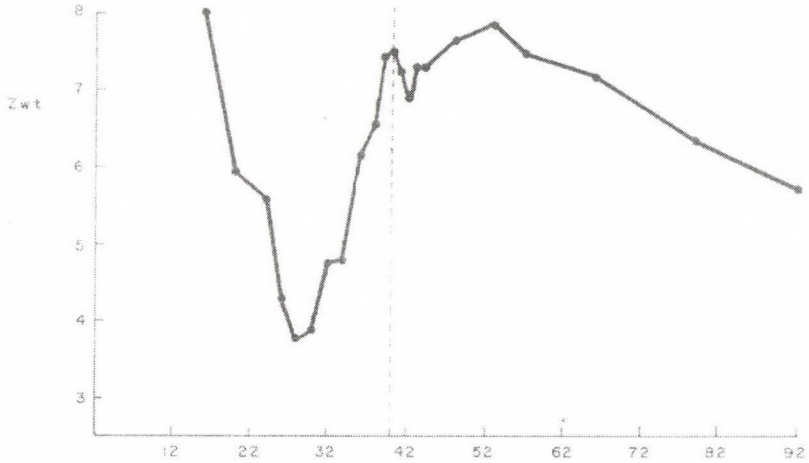


Figure 4: Phantom proportional weight Zwt showing the three months deflection point scaled to weeks from conception on the X-axis.

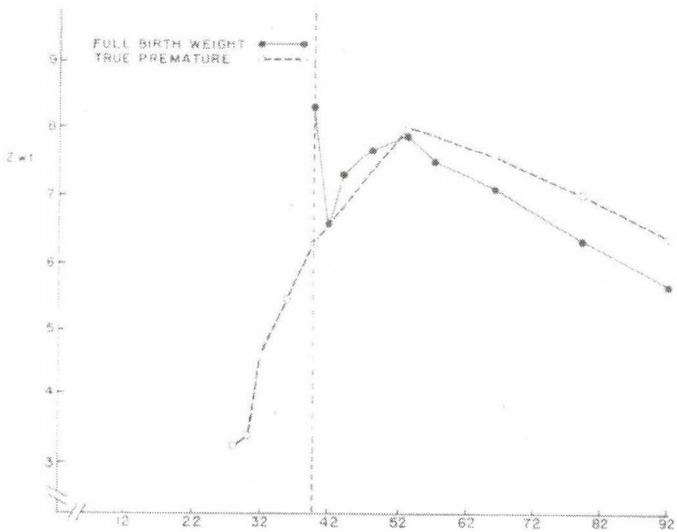
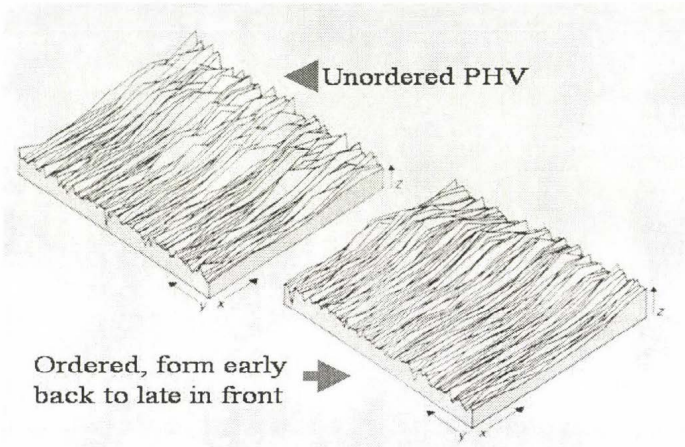


Figure 5: Phantom proportional weight scaled from weeks from conception shown on the x-axis showing very low proportional weight for premature birth but gathering in ponderosity to the peak, postulated as a critical level for the growth to linearity at a slower rate.

Recently, Mary Ross and I restated the hypothesis in *The Phantom Knows* (Ross and Ross in press). We also suggested how it might be explored iconometricographically (age X-axis, proportionality scores Y-axis, and individual subjects on Z-axis) using a tridimensional display piloted by Leahy et al. (1980) for studying growth velocities illustrated in Figure 6. This permits one to look at the pattern for any given order of subjects, or to order the subjects according to the pattern, then use rank order correlation to look at any other variable where there may be a systematic effect that can be tested for the order's predictive index.



Leahy et al. 1980

Figure 6: Tridimensional height velocity display for 100 boys studied annually age 8 to 16 years, Saskatchewan Growth Study, data courtesy Bailey, D.A. Mirwald, R.L. and colleagues.

We like to show this way of using the individual pattern assessment in a sample to intrigue the new generation of human biologists and health professionals. To quote a Zen master: In the beginner's mind there are many possibilities, but in the expert's mind there are few (Shunryu Suzuki).

Commentary

I chose only a small facet of Otto Eiben's over-arching scholarship to show the human dynamics of some research that was initiated and inspired by him. He is one of the greatest anthropologists of his generation. I could have easily have selected any other theme – secular trend (many including Eiben (2003), cross sectional analyses (Eiben, Barabás, Pantó 1991), longitudinal study, unique samples (Eiben and Bodzsár 1990 or his world wide influence in India and many other places. Others, no doubt will touch on these things.

If the world holds together, over 100 and more years from now, Otto Eiben will be regarded with the awe that we have for Adolph Quetelet today. Otto was our friend. He was cultured, kind, thoughtful, generous, and modest human biologist who was loved and admired. He will continue to inspire all of us all our lives and those who follow. He never lost sight of the mission to use science to foster optimal growth, development and

happiness of all the children of all the people and to contribute to the maintenance of health and vigor of adults throughout their life span.

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