IN MEMORIAM
Theodore T. Puck (September 24, 1916–November 6, 2005)

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It is impossible to write a comprehensive obituary of Ted Puck in less than a dozen pages. He was truly a scientist with manifold interests, which included the use of mammalian cell cultures to do quantitative genetic analysis, to determine mutation frequencies, for radiobiology and DNA repair studies, and, finally, to confirm the correct chromosome number of man. Given the limitations of space and my own interests as a cytogeneticist, I have chosen to concentrate on Ted’s interest in the correct number of chromosomes in a normal human cell. Fortunately for me, Ted wrote a wonderful article in the American Journal of Medical Genetics in the section “Living History Biography” (Puck 1994). In this autobiography, Ted Puck summarized the many challenges and successes of his academic and scientific career; I urge everyone who reads this perspective to go to the original!

Ted’s interest in cytogenetics was a direct extension of his interest in using mammalian, especially human, cells as a model for studying mutation and variation. To do this, one needed a reliable method for determining which cells were normal and which abnormal, on the basis, in part, of the karyotype of the individual cells. To appreciate the difficulties that he and other scientists faced at the time, we must transport ourselves back to the middle 1950s. Before 1956, the correct chromosome number of man was assumed to be 48, an assumption based in large part on the studies of Painter (1923) and his use of sections of meiotic cells from human testes. Most karyotypes of human cells in the early 1950s were derived from cancer cells, which were easier to grow in tissue culture than were normal cells. They were wildly abnormal, with many chromosomes including rings and dicentric chromosomes. Then came the astonishing publication by Tjio and Levan in 1956 that reported that the correct number was 46 (Tjio and Levan 1956)! This was confirmed by work done independently by Ford and Hamerton (1956). In each case, a relatively small number of mitotic cells was analyzed; at about the same time, a report by Kodani (1958) suggested that the number differed between whites (46) and Japanese (48).

Ted Puck recruited Joe Hin Tjio to join him in Denver as a graduate student, and together they analyzed >1,800 karyotypes. Fortunately, they were able to confirm the correct number of chromosomes, which was confirmed by work done independently by Ford and Hamerton (1956). In each case, a relatively small number of mitotic cells was analyzed; at about the same time, a report by Kodani (1958) suggested that the number differed between whites (46) and Japanese (48).
mitotic cells from 13 members of the lab who donated a skin biopsy specimen for the project. Clearly before the days of institutional review boards! All except two of the chromosomes were published in the Proceedings of the National Academy of Sciences (Tjio and Puck 1958). Thus, Ted Puck, because of his ability to grow human fibroblasts efficiently, was able to resolve the issue. However, a problem arose because several laboratories that had published papers on the human karyotype used different methods to display and identify them, a difference related, in part, to the systems used to display chromosomes in the species they had studied previously. Thus, for some, it was reasonable to arrange chromosomes with metacentric (more or less) chromosomes lined up from large to small and then acrocentric chromosomes from large to small. Needless to say, some universally accepted system was required to preserve any hope that investigators and the general cytogenetics community could communicate with one another. Remember that all of these developments took place before chromosome banding, so the identification of the individual pairs of chromosomes was based on overall measurement and centromeric index, which often varied quite widely from one laboratory to another (see table 2 of Robinson [1960]).

Ted Puck realized that this confusion would destroy the nascent field of human cytogenetics, but what was to be done? He turned to Charles Ford, who, along with Hamerton, published in 1956 that the correct number was 46 chromosomes. Charles suggested that Puck write to all authors to get their acceptance of a common system. Ted Puck decided that a conference, consisting of all laboratories that had published a human karyotype, would be a more effective way to solve the problem.

In 1960, the participants met in Denver and agreed on the Denver System of Human Chromosome Classification (Denver Conference 1960). The members were an international “who’s who” of human cytogenetics: Lejeune (France); Makino (Japan); Böök, Fraccaro, and Levan (Sweden); Ford, Harnden, and Jacobs (United Kingdom); Chu, Hsu, Hungerford, Puck, Robinson (secretary), Tjio (United States); and counselors Catcheside (United Kingdom) and Stern and Muller (United States). What a gathering this must have been; how one wishes to have been able to eavesdrop on the discussion. The final report was unanimous, and the counselors had nothing to do. At least, that is the impression given by the final report. The chromosomes were grouped in seven sets consisting of relatively similarly sized and shaped chromosomes, numbered pairs 1–22, with the unnumbered X in the third group, 6–12, and the Y chromosome in the smallest group, 21 and 22. Later, the seven groups were given capital letters A–G, and this system was used until chromosome banding was introduced.

It is hard to imagine the field of human cytogenetics without this first conference! A universally accepted framework for nomenclature was absolutely essential! Who would have expected that it was the first of a series of such workshops, each building on the solid foundation of its predecessors? The second conference, in 1966, at the International Congress of Human Genetics in Chicago (Chicago Conference 1966), standardized nomenclature and introduced “p” and “q” (“p” for petite, and “q” with no meaning) (suggested by Lejeune) and other symbols, and the third, in Paris in 1971, combined chromosome banding with the standardized nomenclature (Paris Conference 1971).

Thus, for me, Ted Puck’s unique and most lasting contribution has been to set the field on its way with a logical, universally accepted nomenclature. Equally important was that this order was achieved by consensus of all the players from all of the countries involved. I have participated in the second through fourth conferences, and each of them has followed the pattern established by Ted Puck. We are forever grateful!

I have said nothing about Ted Puck as a person. For me, his success in Denver in 1960 was, in large measure, related to him as a person. He was a gentleman, as defined by Webster’s dictionary: a man who is polite and cultured and has a sense of honor. Given what I know of the sometimes very firm views held by the participants at Denver, it would take someone soft-spoken but quietly determined to get everyone to agree to a uniform classification. I treasure my own interactions with Ted Puck, who showed me how one could be intensely devoted to one’s area of research but never lose the polite and honorable approach to one’s fellow scientists, competitors included. We have all been ennobled by our contact with Theodore Puck.

References

Chicago Conference (1966) Standardization in human cytogenetics. Birth Defects Orig Artic Ser 2