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Josef Warkany's gestation of the teratology society

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Few would dispute that Josef Warkany earned much of the credit for the inception of the first scientific medical teratology society. Warkany once said "*There is not much you can learn about science from history but you can learn much about human nature*". This story is not about the history of this Teratology Society, which was reported by Warkany and others (Brent, 1982; Warkany, 1988a). This story is more personal; it is about Warkany's dreams and aspirations, many of which are reflected in the Teratology Society's roots as well as in the notions implied in its new name "Birth Defects Research & Prevention." What follows are reminiscences that emanated from collegiate and friendly dialogs sustained through several decades and that often focused on our mutual circumstances. I believe that should Warkany have been asked, "Who are you?", his answer would be, "I am I - and my circumstance." Such duality about what is human, as stressed by Jose Ortega y Gasset, looms large in these recollections, and provides a glimpse of Warkany's views of science and medicine that often overflow toward spheres of ethics and humanism. Warkany also expressed such feelings in his etchings and in poetic language that gave rise to his aphorisms. The imperative of brevity calls for limited illustrations, but modern technology offers a remedy in a companion electronic article where Warkany, in his own words, described his circumstances (Wertelecki, 2020) (Figure 1).

Josef Warkany was born in Vienna in 1902, the then capital of the Austro-Hungarian Empire. Vienna also was a hub of political ferment, seething nationalisms and radical ideologies which culminated in the WWI and the fragmentation of the Austrian-Hungarian Empire. Warkany grew up in a rich neighborhood of Vienna that he characterized as a "voluntary ghetto." Not far away, lived Adolf Hitler. Both loved architecture and both failed to pursue that calling. Other nearby residents who impacted Warkany, were Gustav Mahler, Sigmund Freud, and Theodor Herzl. Such circumstances are reflected in Warkany's fondness toward art and suspicion of ideologies, dogmas, and theories which he manifested by saying, "I pursued my dreams on solid grounds" (Wertelecki, 1989) (Figure 2).

Warkany studied medicine at the University of Vienna Medical School, then among the world leading institutions of its kind. He particularly credited Clemens Pirquet for framing his mind; Pirquet admonished Warkany "to pursue what is important". Another mentor was Julius Wagner-Jauregg, a recipient of the 1927 Nobel Prize, whom Warkany described as "a dry and down-to-earth physician, a stable investigator who taught well the right concepts ... whose studies led to the indirect malarial therapy of syphilis". Warkany credited Wagner-Jauregg for his awareness of the cardinal importance of prevention research independently from investigations of causes. In this regard, Warkany once said "*Being ignorant of the causes...such implies that direct prevention is not possible...teratology experiments are endless enterprises...we must reconsider our methods...not only emphasizing frontal attacks but consider less glamorous indirect methods... malformations like all disease and all events in this world – are determined by long chains of causative factors - these chains can sometimes be interrupted by cutting their weak links ....*" An illustration of this principle is flour fortification with folic acid, to reduce the frequency of neural-tube defects, which arguably is the most important public health triumph of the 20th century (Oakley Jr., 2009).

In the 1930s, a prevalent dogma held that the embryo was well protected in the maternal womb from environmental assaults and, therefore, that congenital malformations were reflections of genetic causes, mostly inherited from "flawed" parents. On the other hand, it was well-known, even then, that lack of iodine was teratogenic, depicted by Warkany in an etching he called "Poor in Iodine." This fact propelled Warkany toward

FIGURE 1 Portrait of Josef Warkany during one of his many visits as a distinguished professor to the Department of the College of Medicine of the University of South Alabama in Mobile, Alabama, c. 1980

FIGURE 2 "Substandard Housing, Haydn's Birthplace, Rohrau, Austria," etching by J. Warkany, c. 1961

studies of congenital malformations and mental retardation (Figure 3).

In 1933, Hitler was appointed Chancellor of Germany and enthusiasts of "genetic eugenics," such as Fritz Lenz whose son Widukind Lenz is mentioned later, gain prominence. In the same year, the German "Sterilization Law" (Law for the Prevention of Genetically Diseased Offspring) was enacted, based on the American Model Eugenical Sterilization Act of 1924 largely developed by Harry H. Laughlin (Proceedings, 1928). Two years later, in 1935, the Nuremberg Laws were instituted to promote racist policies. By then, Warkany had already joined the pediatric research team in Cincinnati, nurtured by Dr. Albert Graeme Mitchell. Some called Mitchell and Warkany "the fathers of Scientific Pediatrics and Scientific Teratology" respectively, although neither accepted such titles. One year prior to Warkany's joining the Cincinnati team, Mitchell appointed, among others, Waldo E. Nelson and later, Albert B. Sabin (an immigrant from Poland). Warkany, Nelson, and Sabin became recipients of the prestigious highest honor bestowed by the American pediatric Society for "distinguished service to pediatrics as a whole" (Wilson, 1970).

FIGURE 3 "Poor in Iodine" depicting a family from a mountainous Appalachian region of the US, etching by J. Warkany, c. 1970

After the death of Mitchell in 1941, Nelson assumed the sole editorship of what was then the "Mitchell-Nelson Pediatrics" which has become known as the "Nelson Pediatrics" world-famous pediatrics textbook. In this textbook Warkany presented the progress and his notions of developmental pediatrics and teratology sprinkled with elements of his views of humanism and medical ethics, themes he expanded upon in related publications. Among them, his 1950 article on "Advisability of Parenthood," now referred to as "genetic counseling," the 1951 "Congenital Anomalies," the 1956 "The Role of Congenital Anomalies in the Etiology of Chronic Diseases," and the 1958, "The Need for Parental Counseling in Pediatrics" are epitomes of emerging clinical applications of teratology and human genetics principles. During the 1940–1960 decades, Warkany explored facts and cumulative experiences concerning malformations reported in multilingual sources that appeared in past centuries and recent decades. In 1971, he published an encyclopedic synthesis, his magnum opus he named "Congenital Malformations" with the playful subtitle "Notes and Comments" (Warkany, 1971).

Regarding teratology, starting in 1940, Warkany began to report his scientific observations and challenged the dogma that teratogenesis was inherently genetic in nature. Among his early seminal publications, were his 1940 and 1942 reports concerning "Congenital Malformations Induced in Rats by Maternal Nutritional Deficiencies" (Warkany & Nelson, 1940). The impact of Warkany's studies, combined with the impact of the 1961 tragic epidemic of limb and other malformations, led to the rule of the Food and Drug Administration demanded that medications be tested for potential teratogenic impacts on the embryo. Much of the credit for the discovery that thalidomide, an over the counter medication for "morning sickness" was granted to Widukind Lenz, the son of Fritz Lenz mentioned earlier. Warkany was unconvinced and facts impelled him to write an article of atonement (Warkany, 1988b) (Figure 4).

As a foreign graduate, Warkany had to take a board examination and an unintended consequence of his preparatory studies was the discovery that "Acrodynia," a then well-known, painful and often fatal, worldwide, childhood scourge, could be the result of poisoning by heavy metals. Warkany's research proved his informed intuition to be correct. Acrodynia was the result of the use of teething powders containing mercury. Irrespective of this major scientific achievement, removal of such products from the market was strongly resisted. Commercial interests may have been the source for challenges to Warkany's credibility and even the soundness of his mind. Warkany persisted, the mercury containing powders were removed from the market, and acrodynia vanished (Warkany & Hubbard, 1948, 1951). Warkany remarked "there is nothing as dead as a dead disease"

FIGURE 4 "While the Mother Slept: Thalidomide," etching by J. Warkany, c. 1980

and expressed his feelings in an etching he named, "Silent Triumph" (Warkany, 1966). Many pediatricians today have never heard of acrodynia because it has been eradicated. The notion in "Silent Triumphs" I believe was on Warkany's mind when he conveyed to me the task to safeguard his magnum opus and the collection of reprints of the references sustaining the facts incorporated in his 7-pound magnum opus. At the end of one of his letters on the subject he added "keep me alive" referring to his "7-pounder." Personally, I view Warkany's magnum opus to be one of the classic medical treatises of the 20th century. The synthesis by which Warkany focused on congenital malformations was exacting. Reported facts and experiences are scattered across all medical and other fields as well as across at least several centuries of multilingual sources. Furthermore, such a task demanded not only an expert but a talent to not only to highlight facts but the unknown as well as to produce a harmonious style, sustain clarity and occasional add sprinkles of notions of humanism and ethics. Today, the magnum opus is "out of print" while clinical teratology and genetics emphasis is on the synthesis of recognizable syndromes mostly of unknown etiology and pathogenesis. It is likely, I believe that as scientific advances illuminate new vistas of etiology and pathogenesis, the facts found in the Warkany's 7-pounder will become a valuable asset of facts that will enrich the notions of the nature of structural and functional malformations (Figure 5).

FIGURE 5 "Silent Triumph," demolition of a hospital wing where once children suffering from acrodynia were cared for, etching by J. Warkany, c. 1970

Returning to a focus on the creation of the Teratology Society, Warkany demurred and said "... a premature formalization of an emerging discipline could stunt its growth." In 1957, Warkany was engaged as an advisor to the National Foundation for Infantile Paralysis, headed by Mr. Basil O'Connor, a friend of former President Franklin Roosevelt, who suffered from the disorder. It was then that poliomyelitis, a cause of infant paralysis was being vanquished. Warkany advised that the foundation should shift its attention toward structural malformations. The foundation was renamed as March of Dimes and created the notion "birth defects." In 1959, the foundation appointed consultants, mainly virologists linked to the development of poliomyelitis vaccines, who recommended that the study of inborn errors of metabolism and other genetic problems were of greater interest than studies of structural malformations. Warkany noted – "*How is one to convince virologists of the importance of structural malformations?*" The same year, after a conference in Palm Beach Florida, Warkany, along with Clark Frasier, and Jim Wilson, called for the creation of the Teratology Society. Next year, Warkany was elected its first president and with Wilson presented the scientific principles of teratology. Some 25 years later, Warkany became the first recipient of the March of Dimes Basil O'Connor Award and stated, "I am glad you found me at last!" (Figure 6).

For Warkany, a teratogen was any agent, genetic or environmental in nature that could alter functional or structural embryonal or subsequent development. In this sense, clinical genetics belonged under the umbrella of teratology and not vice-versa. It is self-evident that mental retardation is a cardinal developmental anomaly of concern to teratology, genetics, and toxicology, terms which presently are used somewhat interchangeably. Decades ahead of

FIGURE 6 J. Warkany and B. O'Connor, c. 1959

many others, Warkany recognized mental retardation as posing an equal challenge to both teratologists and geneticists. In 1956, Warkany established a clinic for the "mentally retarded" and in 1957, appointed Dr. Jack Herbert Rubenstein as its director. Together, they developed what became a leading research and care center known as the "Cincinnati Center for Developmental Disorders." This concept evolved and was replicated with presidential support by the development of a number of University Affiliated Programs on Developmental Anomalies.

The depth and scope of Warkany's legacy on the present trends of teratology can be grasped from his dreams and convictions which he conveyed in the third chapter of his magnum opus. Much may have been achieved since then, but much more remains for us to do. Warkany ends this chapter with ... "It seems doubtful that it is necessary in our times to sacrifice the weak for the strong, the retarded for the advanced, and to look at the management of the extremes as alternatives. There are situations in which the physician may doubt that preservation of life of a severely defected child is justified for defensible. But, preservation of life is the physicians task...a charitable attitude towards the weak, the deformed, and the mentally handicapped - irrational as it may seem sometimes to

FIGURE 7 Josef Warkany with Wladimir Wertelecki (c.1987)

clever analysts – apparently has a beneficial effect on the society that maintains it and fosters it. We have witnessed in our lifetime, fine civilizations and sates go down to ruin, destroyed...not by...their weak and deformed, but by well-formed physical specimens whose minds were considered superior by millions of their fellow citizens. Since our society and our laws protect the life of the imperfect child, we must contribute to its care and rehabilitation. It does not seem right to leave the entire financial and emotional burden to the parents, whose misfortune is undeserved. Abnormal children teach us a great deal ... To contribute to their care is the price to be paid by those who have normal children – the price to be paid for overcoming their barbarism and cruelty inherent in the societies that eliminate the weak and dispose of the deformed" (Warkany, 1971). Perhaps this chapter should be a pathfinder for those entering the field of teratology.

Warkany left us in 1992, and this account seeks to fulfill, in part, his plea "keep me alive." This task is enlivened when we hear his voice, glance at his etchings, and grasp the depth of his adages contained in an electronic companion article (Wertelecki, 2020) (Figure 7).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Brent, R. L. (1982). Biography of Josef Warkany. *Teratology*, *25*(2), 137–151.

National Conference on Race Betterment; Race Betterment Foundation, 1928 Proceedings of the third Race Betterment Conference, January 2–6, 1928: under the auspices of the Race Betterment Foundation, Battle Creek, Michigan.

Oakley, G. P., Jr. (2009). The scientific basis for eliminating folic acid-preventable spina bifida: A modern miracle from epidemiology. *Annals of Epidemiology*, *19*(4), 226–230. https://doi.org/10.1016/j.annepidem.2009.01.016 Review.

Warkany, J. (1966). Acrodynia–postmortem of a disease. *American Journal of Diseases of Children*, *112*(2), 147–156.

Warkany, J. (1971). *Congenital malformations: Notes and comments*. Chicago, IL: Year Book Medical Publishers, Inc.

Warkany, J. (1988a). Story of a Teratologist. In H. Kalter (Ed.), *Issues and reviews in teratology* (Vol. 4, pp. 1–79). New York: Plenum Publishing Corp.

Warkany, J. (1988b). Why I doubted that thalidomide was the cause of the epidemic of limb defects of 1959 to 1961. *Teratology*, *38*(3), 217–219.

Warkany, J., & Hubbard, D. M. (1948). Mercury in the urine of children with acrodynia. *Lancet*, *1*(6509), 829.

Warkany, J., & Hubbard, D. M. (1951). Adverse mercurial reactions in the form of acrodynia and related conditions. *A.M.A. American Journal of Diseases of Children*, *81*(3), 335–373.

Warkany, J., & Nelson, R. C. (1940). Appearance of skeletal abnormalities in the offspring of rats reared on a deficient diet. *Science*, *92*(2391), 383–384.

Wertelecki, W. (1989). Of dreaming on solid grounds and silent triumphs of one man: A story about Josef Warkany. *American Journal of Medical Genetics*, *33*(4), 522–536.

Wertelecki, W. Josef Warkany Speaks of Teratology. E-article, 2020: http://medword.net/carousel/carousel.php?id=7.

Wilson, J. G. (1970). Presentation of the Howland award of Josef Warkany. *Pediatric Research*, *4*(5), 427–430.

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