



Josef Warkany – Teratology Then and Now
Expanded Version

W. Wertelecki, M.D.

**Presented at the 50th Anniversary of the Teratology Society Meeting
Louisville, KY, USA (June 2010)**

Note: This expanded version of the oral presentation is expanded by six video clips and comments by the author. To view the videos, please click on the hyperlinks and the return arrow (upper left) to continue. To display the comments, place the arrow-cursor on the icon on the upper left corner. Please also note that reproduction/dissemination of contents and illustrations requires written permission.

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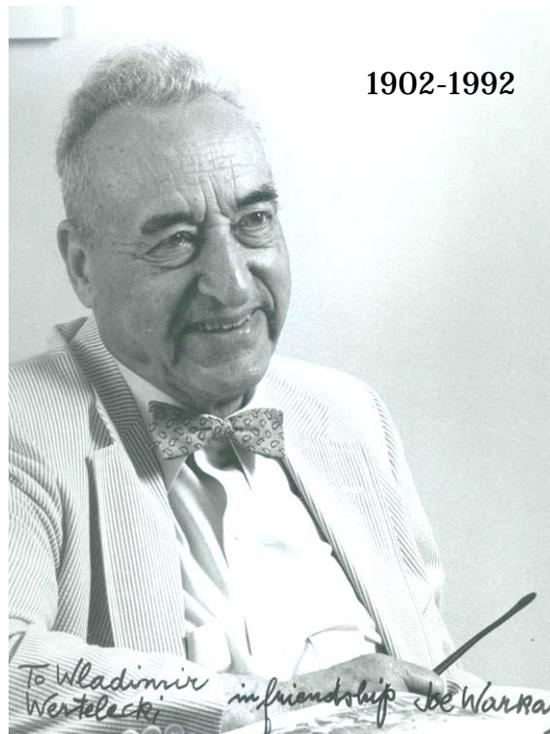


The author has no financial or other interests which pose a conflict of interest concerning this presentation.

Video recordings were kindly provided by the Edward L. Pratt Library of the Cincinnati Children's Hospital

This presentation is based on

A Story about Josef Warkany
"Of Dreaming on Solid Grounds"



W. Wertelecki, M.D.
Am J. Med. Genet., 33: 522, 1989
(genfir3@gmail.com)

THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS, INC.

FRANKLIN D. ROOSEVELT, FOUNDER

120 BROADWAY

NEW YORK 5, N. Y.

BASIL O'CONNOR
PRESIDENT

January 14, 1957

Josef Warkany, M.D.
Professor of Research Pediatrics
Children's Hospital
Cincinnati, Ohio

Dear Doctor Warkany:

I am indeed pleased that you are able to arrange your schedule so that you might work with us for a period of approximately two months for the purpose of assisting us in investigations we are making on future program studies for the National Foundation for Infantile Paralysis.

THE NATIONAL FOUNDATION
FRANKLIN D. ROOSEVELT, FOUNDER
800 SECOND AVENUE
NEW YORK 17, N. Y.

BASIL O'CONNOR
PRESIDENT

April 21, 1960

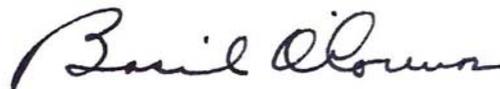
Dear Dr. Warkany:

I was greatly pleased to learn from your letter of April 14 of the formation of a Teratology Society in New York City on April 10, 1960.

Knowing as you do The National Foundation's interest and developing activity in the field of congenital malformations, I think you are aware of our desire to cooperate with your Society in every way we can.

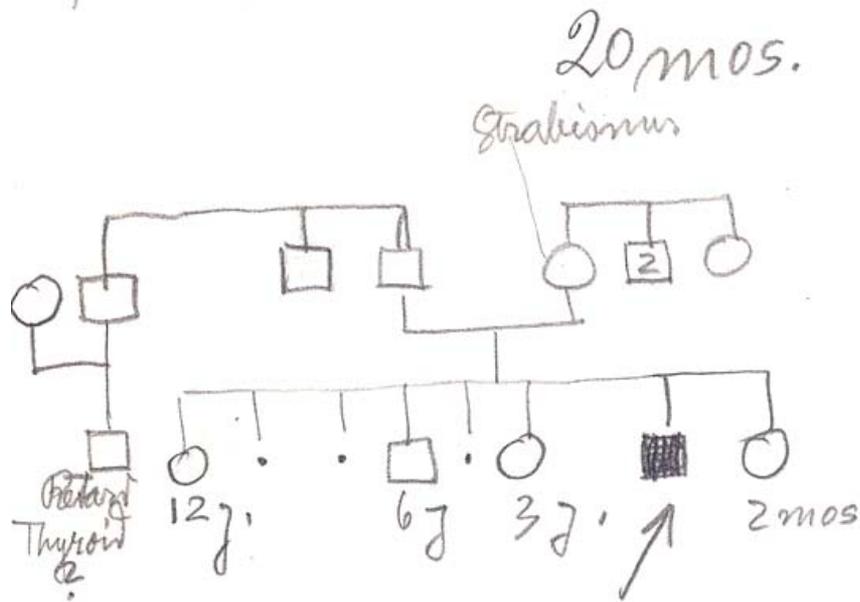
I want to extend to you, as President, and to the other officers The National Foundation's good wishes for the success of the Teratology Society in its important health field.

Sincerely yours,



President

Dr. Josef Warkany, President
Teratology Society
The Children's Hospital Research
Foundation
Cincinnati 29, Ohio



Mother Rh neg.
Father Rh pos.

Pregnancy not remarkable
9 mos. - Was active

B.D. 5/28/58

1505 West Main St
Loveland, O.

NO. 4-2091

F: Kyle, 37y.

M: Betty, 37y.

No consanguinity

Misc. 1950, 1952, 1956

No illness, No G.M. -
in utero like older children

politicians, lobbyists and administrators have become interposed between the granting agency and the investigator. Many investigators have been forced to become admin. & politicians with varying results

Of course, I am guilty
of many exaggerations and
~~but~~ extrapolations but
what can you expect from
an investigator who
began his work with a
single rabbit?

The investigator. Many
investigators have been forced
to become admin. & politicians
with varying results



1902-1992

A Story about Josef Warkany
["Of Dreaming on Solid Grounds"](#)

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Ego sum
"Me"

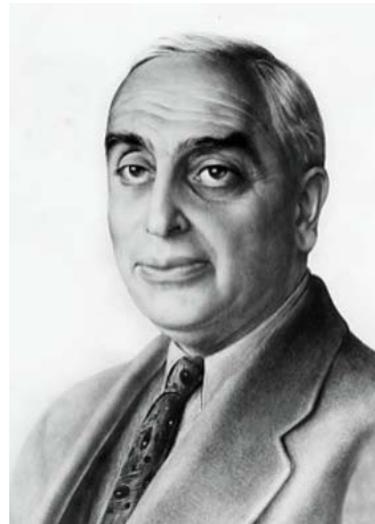
ORIGINAL
SYNCRETIC
ARTIST
POINEER
LEADER
IDEALIST
HUMANIST
HUMORIST
CRITIC
AUTHOR
PHYSICIAN
DISCOVERER
SCIENTIST
RESEARCHER
CLINICIAN
TERATOLOGIST

My Circumstance

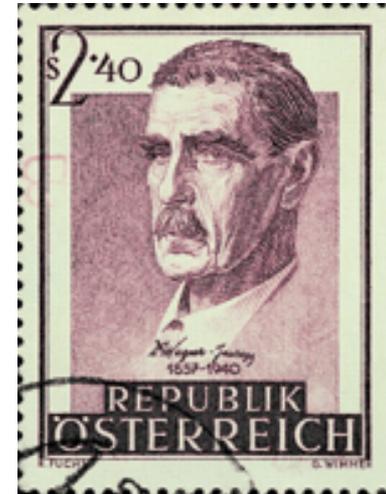


Clemens P. F. von Pirquet

Pirquet



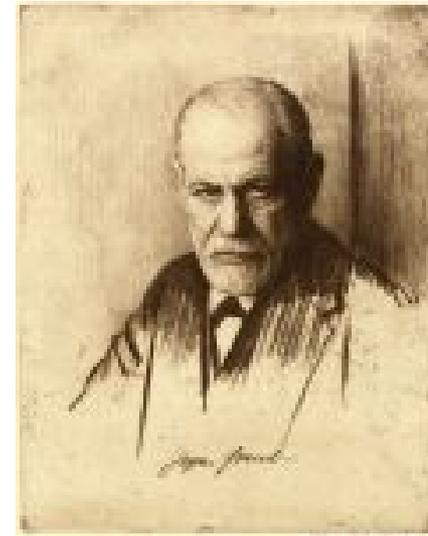
Bela Schick



Julius Wagenr-Jauregg



Josef Warkany
Vision
Humanism-Prevention
(Indirect approaches)
Congenital anomalies
(Mini – Macro)
Mental retardation



To view please click on the link

http://www.medword.net/flash/1988_wark1/

**“Ego sum” (and my circumstance – Vienna 1900-1933)
... “genetic counseling” then.**



"Unless the hospital is interested in the prevention as well as the cure of disease, unless effort is made to study and investigate problems in a manner which will add in a constructive way to existing knowledge, we have all of us failed to function to the fullest extent."

A. Graeme Mitchell, MD



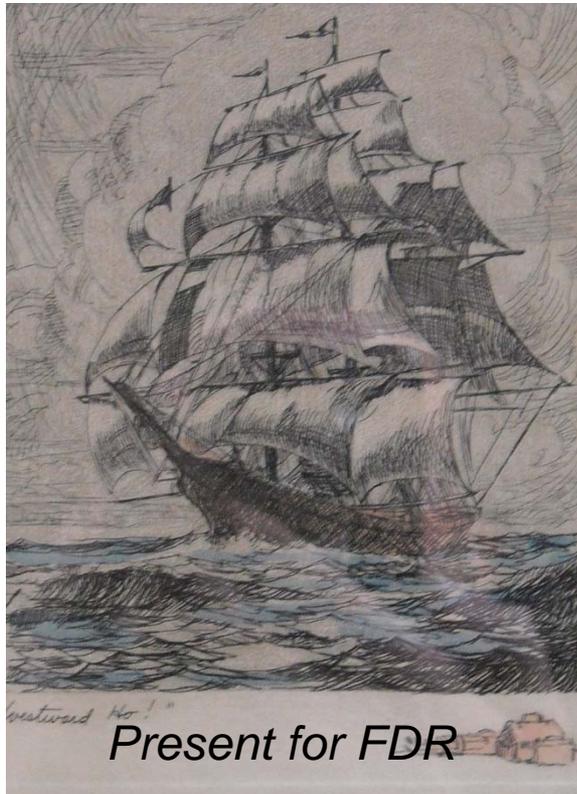
*Board President of the Children's Hospital in Cincinnati (**donated \$2.5 million** for the building and endowment of the Cincinnati Children's Hospital **Research Foundation** – created the first profit-sharing program for employees in the U.S.)*

William Cooper Procter

To view please click on the link

http://www.medword.net/flash/1980_wark1_a/

“Ego sum” (an my circumstance – Cincinnati 1933 ...
“ *... what if I would take-up endocrinology ...
most of the patients ...
were patients with congenital malformations ...* ”



Etching and watercolor by G. Mitchell, M.D.



PandoraWordBox.com



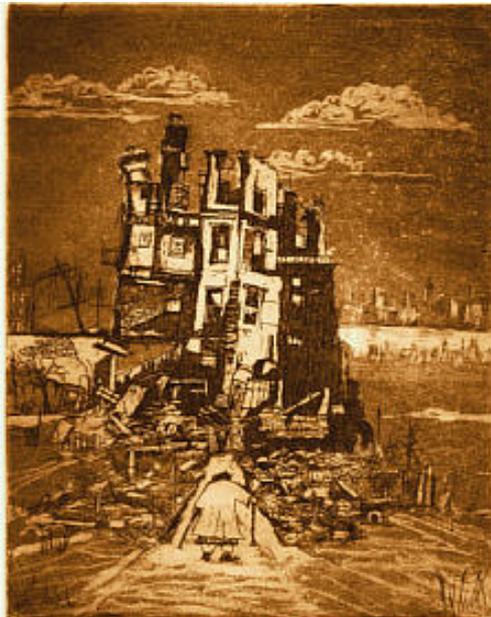
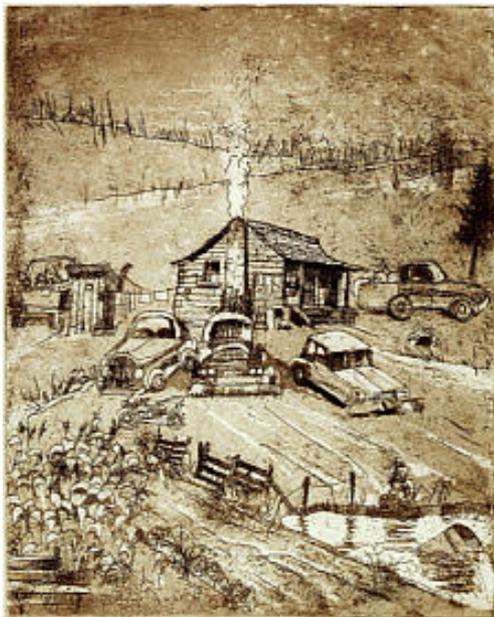
Child of Non-Disjunction



A Patient's Point of View

(“Affective Poverty - Emotional Deficits”)

“ ... patients ... were treated ... as objects ... it helped to depress and humiliate the ... patient more than necessary. ”



To view please click on the link

http://www.medword.net/flash/1980_wark2/

Science and Humanism

***“ ... involved in the mental retardation
movement ... parents organizations “***



Poor in Iodine



To view please click on the link

http://www.medword.net/flash/1980_wark1_b/

Failure – Victory – Scientific Medical Teratology

“... we failed completely ...

but we found something much better ...”



W. Nelson

The "Illiad" of Josef Warkany

MITCHELL-NELSON

Textbook of Pediatrics

1940's

*Endocrinology > Cretinism > Iodine
Prevention*

*Prenatal factors > Congenital Anomalies
Maternal > Fetal Nutrition*

Mental Retardation > Malformations

Advisability of Parenthood. " ...explain to the prospective parents the chances of having normal and abnormal children and then let the parents make their decision ... **the embryo-fetus should be assured protection from adverse environmental influences** ... why the **prejudice** by **calling such** (advisory services) **genetic counseling**" ...

Josef Warkany's 25 year long "Odyssey"

CONGENITAL MALFORMATIONS

Notes and Comments

JOSEF WARKANY, M.D.
*Fellow of The Children's Hospital Research Foundation, Cincinnati, Ohio
Professor of Research Pediatrics, University of Cincinnati*

Notes and Comments:
Facts plus personal views.

("I did not merely copy what others had written before ...")

1971

LAST (Medical) "CLASSIC"

"In 1945 ... I thought that 2 years would be sufficient time for writing such a book, but it actually took 25 years ... I pointed out that the ancient **history of teratology** does not teach us much about the origin of congenital malformations but it tells us much **about the human mind** and its reactions to unexplained phenomena ..."



MYTH-(thanatic) REPORT
(“birth defects” are not solely due to genetic flaws)

Reprinted from SCIENCE, October 25, 1940, Vol. 92,
No. 2391, pages 383-384.

APPEARANCE OF SKELETAL ABNORMALI-
TIES IN THE OFFSPRING OF RATS
REARED ON A DEFICIENT DIET

MATERNAL - FETAL NUTRITION

(1945) “ ... experiments indicate that congenital malformations may be caused by maternal nutritional deficiency.



The Demise of Acrodynia (a)

*(1966) ... children presented **symptoms** somewhat **out of the ordinary** and yet all so **much alike** that they could safely be called the same condition ... more like a **low-grade toxemia** ... established that acrodynia was due to **exposure to mercury** ... acrodynia died an inglorious death ... (28 years later) ...*

To view please click on the link

http://www.medword.net/flash/1980_wark3/

Humanism – Science – Public Health Victory
The story of Acrodynia
“Nothing is as dead as a dead disease ...”



The Demise of Acrodynia (b)

*(1966) ... mercury was removed as an ingredient of teething powders ... another toxic agent was introduced to replace mercury ... (societies) do not abandon time-honored customs without **risk of penalty** ...”*

APS-SPR Howland Award Recipients



Fig. 7. a: Learning surgery (Vienna, 1927). b: On board *SS Deutschland* from Hamburg to New York (1931). c: Waldo E. Nelson, Clement A. Smith, Charles A. Janeway, Helen B. Taussig, Harry H. Gordon,

Albert B. Sabin, and Josef Warkany during a Howland Awardees Dinner (1978).



TERATOLOGY

Care - Prevention - Medicine - Civilization

Indirect Approaches

*“Malformations, like all diseases – and all events in this world – are determined by **long chains of causative factors**, and these chains can sometimes be interrupted by cutting their weak links ...”*

*“... objection I have is to the attitude (of those) who contend that (research of causes and mechanisms) is the most ... “sophisticated” (an approach deserving first priority) ... **“unsophisticated” observations** have sometimes **led to the prevention of congenital malformations ...”***

*“The **care** of the malformed and **prevention** of malformations ... is the **price of civilization**” (paraphrased)*

“ ... how is one to convince virologists (geneticists) of the importance of malformations?”

“ ... we worked together in 1957 at the National Foundation of Infantile Paralysis

“ ... our proposals were accepted and “birth defects” became the subject of activity of the National Foundation ...

*“There exists ... an almost **religious belief** in the powers of **molecular alchemy** ...”*



B. O'Connor – J. Warkany

http://www.medword.net/flash/1987_wark2/

“Father of Teratology ...”

1959



Fig. 11. With Basil O'Connor (c. 1959).



Fig. 12. Giving the signal to establish a teratology society during a meeting in Palm Beach, Florida (1959)

1961

TERATOLOGY SOCIETY

On April 9-1-, at New York, NY, a Fourth Teratology Conference was held ... 62 of 93 invited participants attended the business session ... for the purpose of organizing (the society) ... elected by acclamation: President, Josef Warkany; President-Elect, James G. Wilson, ...



Josef Warkany – Teratology Then **and** Now

*“ ... a need exists for **longitudinal studies of the natural history** ... to attract attention to prenatal factors ... to stress the need for reorientation in the research concerned with the prevention ... ”*

*“ ... we must attempt **indirect methods of prevention** ... it must be realized that ... **experimentation with teratologic mechanisms are endless enterprises ... seldom useful in prevention ... ”***

(“ There is no proof yet that microcosmic (molecular) research on congenital malformations will lead to teratologic prophylaxis. ”)

(... \$3 billion Human Genome Project ... “Genetic Map Yields Few New Cures ... perhaps in another 15 to 20 years ... (pharmaceutical) industry researchers urge a wait-and-see patience ... ” - New York Times - June 12 and 14, 2010)



Teratology Now

Malformations in a Chernobyl-Impacted Region

Anencephaly
 Conjoined *Twins*
 Sacrococcygeal
 Teratomas
 (excess of females)

Peds 2010: 125; e836.

| | EUROCAT | UKRAINE |
|-----------------------------|---------|---------|
| Neural tube defects | 10.2 | 18.5 |
| Anencephaly and similar | 3.8 | 8.1 |
| Microcephaly | 2.3 | 6.0 |
| Anophthalmia-Microphthalmia | 1.4 | 2.3 |
| Congenital cataract | 1.0 | 2.2 |
| Tetralogy of fallot | 3.0 | 2.7 |
| Cleft lip w/without palate | 9.6 | 10.6 |
| Cleft palate | 6.1 | 5.0 |
| Limb reduction | 5.7 | 5.6 |

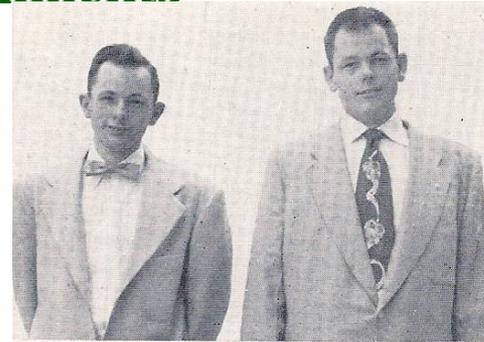


| Anomaly | Contaminated Raions (Polissia) | Untaminated Raions (not Polissia) | P-value ^a |
|----------------|--------------------------------|-----------------------------------|----------------------|
| Births (n) | 43,392 | 53,046 | |
| NTDs | 27.0 | 18.3 | 0.003 |
| Microcephaly | 3.7 | 1.3 | 0.02 |
| Microphthalmia | 1.8 | 0.4 | 0.03 |

Note: much of “Teratology Then” is “Teratology Now” – for example, our investigation of Chernobyl impacted populations demonstrates elevated rates of Conjoined Twins – Teratomas - NTD – Microcephaly – and Micorphthalmia – a review of “Teratology Then” summarized by Warkany is illuminating (see next)

Teratology – Then and Now Warkany’s “Notes and Comments”

(1951) “**Dissimilarity of MZ twins** ... non-genetic deviations of metabolic processes of **embryonic organizers.**”



(1950-1960) **Hemihypertrophy** ... most plausible etiology ... is a faulty **cell division of the zygote** ... daughter cells of unequal size ... form of incomplete **twinning. Females** are more often affected ... **right side** of the body is involved more frequently ...

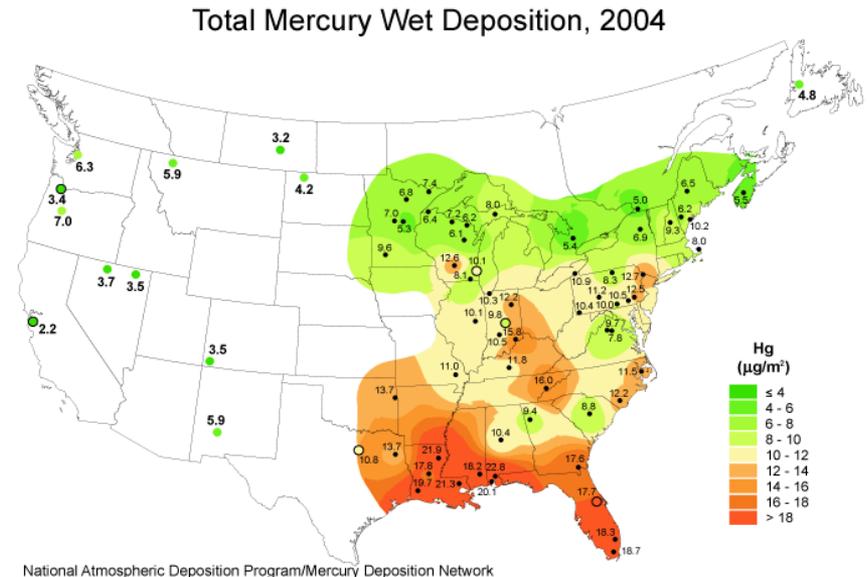
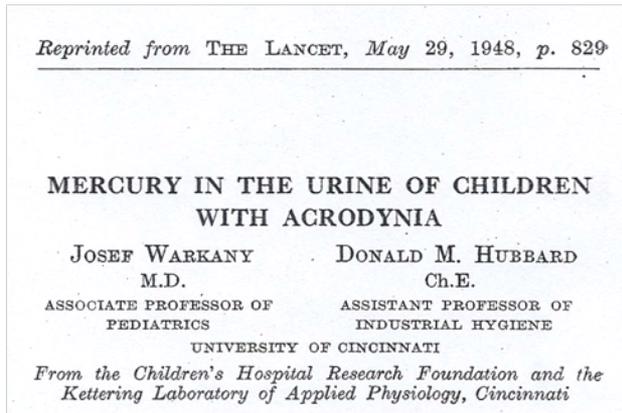


(1961) Some positive indication that (genetic **damage on populations exposed to the atomic bombs**) was forthcoming from analysis of sex ratio in the off-spring (**excess of females**)

DISASTERS

Minamata Bay Acrodynia Chornobyl BP-"Chornobyl"

Radiation - Petrochemicals - Mercury - Arsenic ... Teratology "Now"



Etchings and articles by Warkany about the disasters of Hiroshima, Nagasaki, Minamata Bay and Acrodynia show how he was touched by these tragedies. Now we are confronted with large populations exposed to Chornobyl, low doses of ionizing radiation, mercury pollution and the massive petrochemical pollution of the Gulf of Mexico. A retrospective glance to Teratology "Then" may invigorate Teratology "Now".

End