

# History of mistletoe therapy in the context of the development of modern oncology

Marion Debus

# Rudolf Virchow 1821-1902



- 1858: „Cellular pathology“
- 1862: „Die Krankhaften Geschwülste“  
(The Pathological Tumors)

# Stephen Paget 1855 -1926



- In 1889 „Seed and soil“ hypothesis
- Questions the „centrifugal theory“ of cancer growth prevailing at his time
- Up to the present day no „met genes“ were discovered

“.....as ambitious cancer researchers study soil as well as seed, one sees the beginnings of a new approach. It would return us to the true meaning of “holistic”: to take the body, the organism, its anatomy, its physiology—this infuriatingly intricate web—as a whole.”

Cancer's Invasion Equation | The New Yorker

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THE  
NEW YORKER

ANNALS OF MEDICINE SEPTEMBER 11, 2017 ISSUE

# CANCER'S INVASION EQUATION

*We can detect tumors earlier than ever before. Can we predict whether they're going to be dangerous?*

By Siddhartha Mukherjee

# William Stewart Halsted 1852-1922





# William B. Coley 1862-1936







**Elisabeth Dashiell** (*Bessie*), confidant and close friend of John D.

Rockefeller Jr, was diagnosed with a highly aggressive round cell sarcoma, and despite radical surgery and in spite of Coley's intensive care, there was rapid progression and Elisabeth died a few months later ..... this set into motion Coley's research and work

From that day on Rockefeller (and later his foundation) always supported Coley's work; the CRI , founded by Nauts & Loyd – was supported by this.



Signor Zola, who survived another 8 years after being treated by Coley in 1891



# Wilhelm Conrad Röntgen 1845 -1923



- Discovers X-rays in 1895
- 1896 first radiotherapy of locally advanced breast cancer by Emil Grubbe in Chicago

# Attitudes towards cancer immunotherapy

- 1900 – 1950: No immunotherapeutic approaches in mainstream medicine:
  - ⇒ Difficult to reproduce tumor regression with Coley's toxin
  - ⇒ Treatment highly toxic
  - ⇒ No accepted theoretical framework for cancer immunotherapy
  - ⇒ BUT: Paul Ehrlich suggests in 1909 that immune system may control cancers!

# Rudolf Steiner 1861 - 1925



# Ita Wegman 1876 - 1943



## Mistletoe therapy – first steps

- Steiner mentions mistletoe as a remedy repeatedly in lectures since 1904
- 1916 Steiner describes process of cancer as *acceleration* and mistletoe-process as *retardation*
- 1917 Wegman treats her first patients in Zurich with *Iscar* with good results
- 1920 – 1924 Steiner repeatedly talks to doctors about cancer and mistletoe treatment from various points of view

# Concept of Anthroposophic Cancer treatment in 1920

- Cancer is a systemic disease
- Cancer affects whole human being in all his dimensions (body, soul, spirit)
- Mistletoe therapy = „Immunotherapy“:
  - => „Sheath of warmth“ around tumor should be created (local aspect)
  - => No result to be expected unless fever is being induced (systemic aspect)





6489 Klinik Arlesheim  
(Gesamtansicht)



# Klinik Arlesheim

Akutklinik für  
Innere Medizin,  
Onkologie,  
Psychiatrie und  
Psychosomatik



# „Klinisch Therapeutisches Institut“

- 1921 Opening of „*Klinisch-therapeutisches Institut*“, first anthroposophic hospital, in Arlesheim by Ita Wegman
  - ⇒ Emphasis on development of cancer treatment, especially mistletoe therapy
  - ⇒ *Integrative, interprofessional treatment* is being developed: Nutrition, rhythmical massage, baths, external applications (compresses, embrocations), art therapy, curative eurythmy
  - ⇒ Cancer is the result of a decade long process: How can the patient be adressed on all levels – spirit, soul, body – to achieve a thorough healing process?
  - ⇒ Research was estimated crucial and intended from the beginning

„Ein neues Mittel gegen Carcinom“ („A new remedy against cancer“)

Eberhard Schickler 1924

22 case histories on Iscador Treatment:

- I.: Inoperable conditions
- II.: Adjuvant treatment
- III.: Prophylactic treatment

„Ein neues Mittel gegen Carcinom“ (A new remedy against cancer)

Eberhard Schickler 1924

- Viscum-concentrations 0,5%, 1%, 3%, 5%, 10% (20%)
- Given in series every other day for two weeks
- Injection near tumor or even intratumoral
- Mild fever reaction should be achieved
- Ongoing treatment for longer periods of time, sometimes for years, with breaks in between

„Ein neues Mittel gegen Carcinom“ („A new remedy against cancer“)

Eberhard Schickler 1924

Results:

I.: Inoperable conditions:

- Marked improvement of general condition (less fatigue, weight gain, improvement of sleep and appetite, able to work again)
- Tumor remissions
- Late palliative stage: Improvement of quality of life, reduction of pain

„Ein neues Mittel gegen Carcinom“ („A new remedy against cancer“)

Eberhard Schickler 1924

Results:

II.: Adjuvant treatment:

- Patients much stronger, less fatigue
- Side effects of radiotherapy can be avoided
- Risk of recurrence reduced



„Ein neues Mittel gegen Carcinom“ („A new remedy against cancer“)

Eberhard Schickler 1924

Results:

III.: Prophylactic treatment:

Patients characteristics:

- Very tired, sleeping disorder, constipation, accelerated aging, dry skin.
- Symptomatic treatment not successful, family history of cancer
- Patients stronger, less anxiety, come back on their own asking for the injections

## First scientific steps in mistletoe evaluation

- 1938 Fr. E. Koch: Successful treatment with *local intratumoral injections* of the mistletoe preparation Plenosal in animal models
- 1948 First description of Viscotoxins
- 1955 Chernov shows in rabbits, that *systemic intravenous application* of the mistletoe preparation Omelan can also reduce local tumor growth and can reduce metastases in number and size
- 1956 discovery of Mistletoe Lectins
- Already since the 1960ies the immunological properties of Mistletoe preparations are extensively studied in vitro and in animal experiments

Alexandre Leroi 1906-1968



# Alexandre Leroi 1906-1968

- Dedicated his life to the fight against cancer
- Important encounter with Rudolf Steiner as a Waldorf School pupil in Stuttgart
- Joins Klinik Arlesheim (Klinisch Therapeutisches Institut) in 1934
- Improves manufacturing process of Iscador, with better temperature reactions and better tolerability as a result
- Founder of Research Institute „Hiscia“ in Arlesheim 1949
- Since 1952 increasing amount of publications
- Opening of „Lukas Klinik“ in Arlesheim in 1963

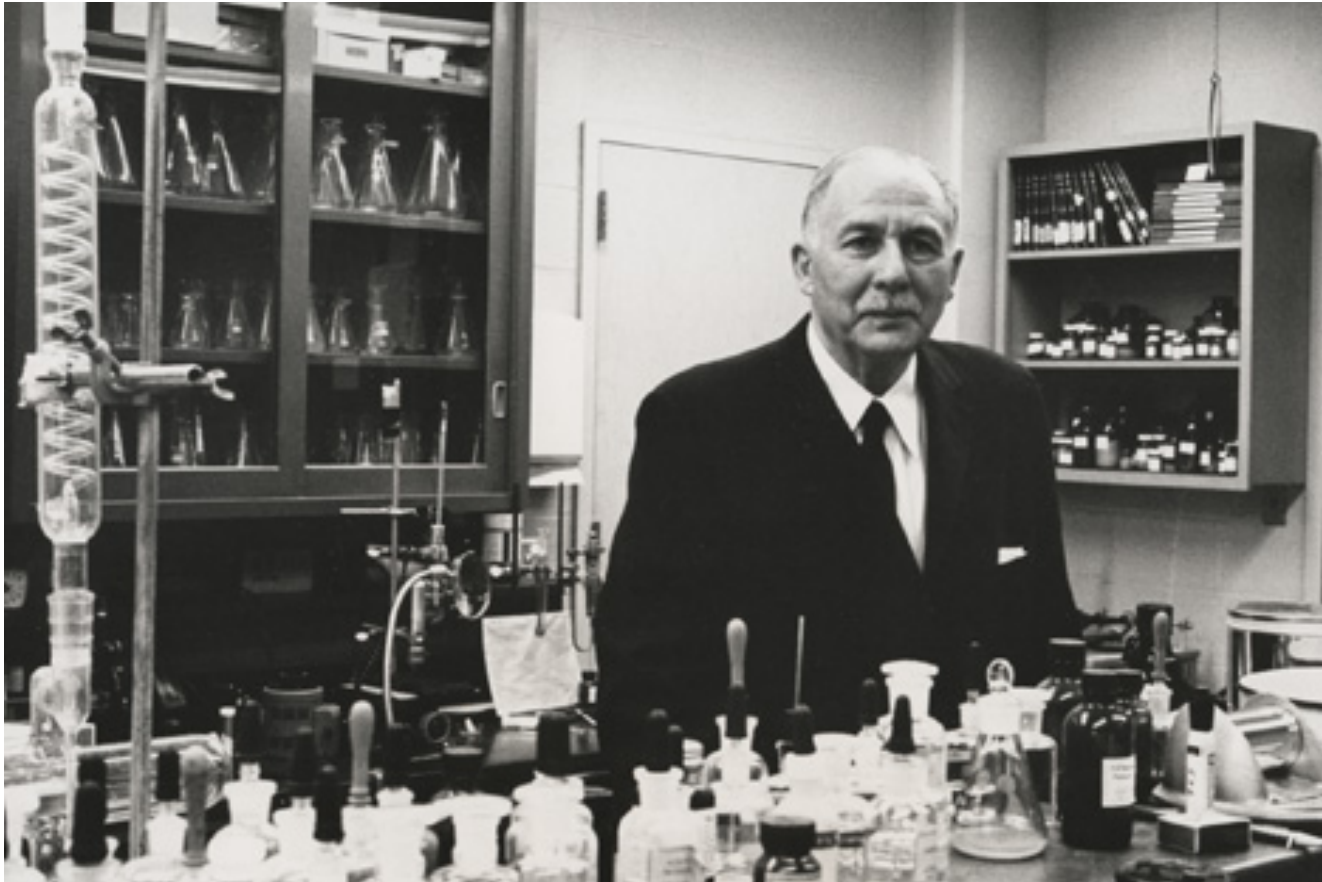
# Georg Salzer 1903 - 1995

- Short encounter with Rudolf Steiner as a student, was deeply impressed
- Professor for Surgery in Vienna 1953-1968
- Implemented the first heart-lung-machine in Vienna
- Defined the staging system for lung cancer in 1949
- Developed the revolutionary method of breast-maintaining segment- or quadrantresection in the 1950ies (!)
- Implemented mistletoe treatment in the oncologic outpatient clinic in his hospital

# Georg Salzer 1903 - 1995

- Systematic scientific workup of mistletoe treatment in his department, first randomized trials
- Showed better outcome for adjuvant mistletoe treatment in breast-lung- and stomach cancer.
- Statistical significant advantage of mistletoe treatment for more advanced stage (lymphnodes involved)
- Pleural effusions successfully treated with intrapleural mistletoe instillations

# Sidney Farber 1903-1973





# The New England Journal of Medicine

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## TEMPORARY REMISSIONS IN ACUTE LEUKEMIA IN CHILDREN PRODUCED BY FOLIC ACID ANTAGONIST, 4-AMINOPTEROYL-GLUTAMIC ACID (AMINOPTERIN)\*

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ROBERT F. SYLVESTER, JR., M.D.,¶ AND JAMES A. WOLFF, M.D.||

BOSTON

**I**T IS the purpose of this paper to record the results of clinical and hematologic studies on 5 children with acute leukemia treated by the intramuscular injection of a synthetic compound, 4-aminopteroylglutamic acid (aminopterin). This substance is an antagonist to folic acid regarding the growth of *Streptococcus faecalis R.*

ment of leukemia were obtained from studies on a four-year-old girl with a rapidly progressing acute myelogenous leukemia.<sup>2</sup> Treatment from February 17 to March 24, 1947, with pteroyldiglutamic acid (diapterin), in a dosage of 100 to 300 mg. intramuscularly daily, had no effect upon the hematologic picture. The patient appeared to be moribund. A

## Frank Macfarlane Burnet 1899-1985



The idea of man as the dominant mammal of the earth whose whole behaviour tends to be dominated by his own desire for dominance gripped me. It seemed to explain almost everything, and I applied it to everything.

— *Frank Macfarlane Burnet* —

# Frank Macfarlane Burnet 1899-1985

- 1949 Theory of acquired immunological tolerance
- 1967 Cancer immunosurveillance theory  
=> search for tumor-associated antigens (TAA)

## AUTO-IMMUNITY AND AUTO-IMMUNE DISEASE

*A survey for physician or biologist*

SIR MACFARLANE BURNET

MTP  
MEDICAL AND TECHNICAL  
PUBLISHING CO LTD  
1970

## IMMUNOLOGICAL SURVEILLANCE

SIR MACFARLANE BURNET

*Emeritus Professor of Experimental Medicine  
University of Melbourne*



PERGAMON PRESS  
OXFORD, LONDON, NEW YORK, TORONTO, SYDNEY

# 1969 Gemeinschaftskrankenhaus Herdecke founded by Gerhard Kienle





23.12.1971:  
President Richard Nixon signs National Cancer Act and declares war on  
cancer



## New manufacturers of Mistletoe preparations

- 1971 ABNOBA
- 1975 HELIXOR

# NSABP-04 trial 1981

- Recruiting for ten years in thirty-four centers!
  - No collaboration from surgeons
- ⇒ Rates of breast cancer recurrence, distant cancer metastasis and death statistically identical between radical mastectomy and simple mastectomy



# Attitudes towards cancer immunotherapy

- Since 1995: Immunotherapeutic approaches regarded as promising:
  - ⇒ Dendritic cells can present TAA to the adaptive immune system
  - ⇒ Emergence of the innate immune system as an important mediator of antitumor immunity
  - ⇒ Immunosurveillance hypothesis is resurrected and developed further by „The three Es of cancer immunoediting” (Dunn, 2002 and 2004)
  - ⇒ “Hallmarks of Cancer Next Generation”: for the first time evasion of immune destruction as organizing principle of neoplastic disease recognized (Hanahan & Weinberg 2011)

# Intralesional Mistletoe treatment

- 1996 Scheffler et al.: Complete remission of a squamous cell cancer of the oral cavity: 1,8 cm tumor, treated with 15 intralesional injections of AbnobaViscum Fraxini for 12 weeks => complete remission after highly inflammatory response
- 1996 von Laue: Regression of brain metastases for two times after intralesional injection with AbnobaViscum Fraxini in two subcutaneous metastases of malignant melanoma

**=> Direct cytotoxicity AND change of immune response**



CASE REPORT

## Durable Regression of Primary Cutaneous B-Cell Lymphoma Following Fever-inducing Mistletoe Treatment: Two Case Reports

Maurice Orange, MSc; Aija Lace; Maria P. Fonseca; Broder H. von Laue, Dr med; Stefan Geider, Dr med; Gunver S. Kienle, Dr med

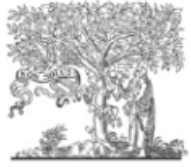
Clinical Case Report

Medicine<sup>®</sup>

OPEN

### Complete remission and long-term survival of a patient with melanoma metastases treated with high-dose fever-inducing *Viscum album* extract A case report

Paul G. Werthmann, MD<sup>a,\*</sup>, Alexander Hintze, MD<sup>b</sup>, Gunver S. Kienle, MD<sup>a,c</sup>



ELSEVIER

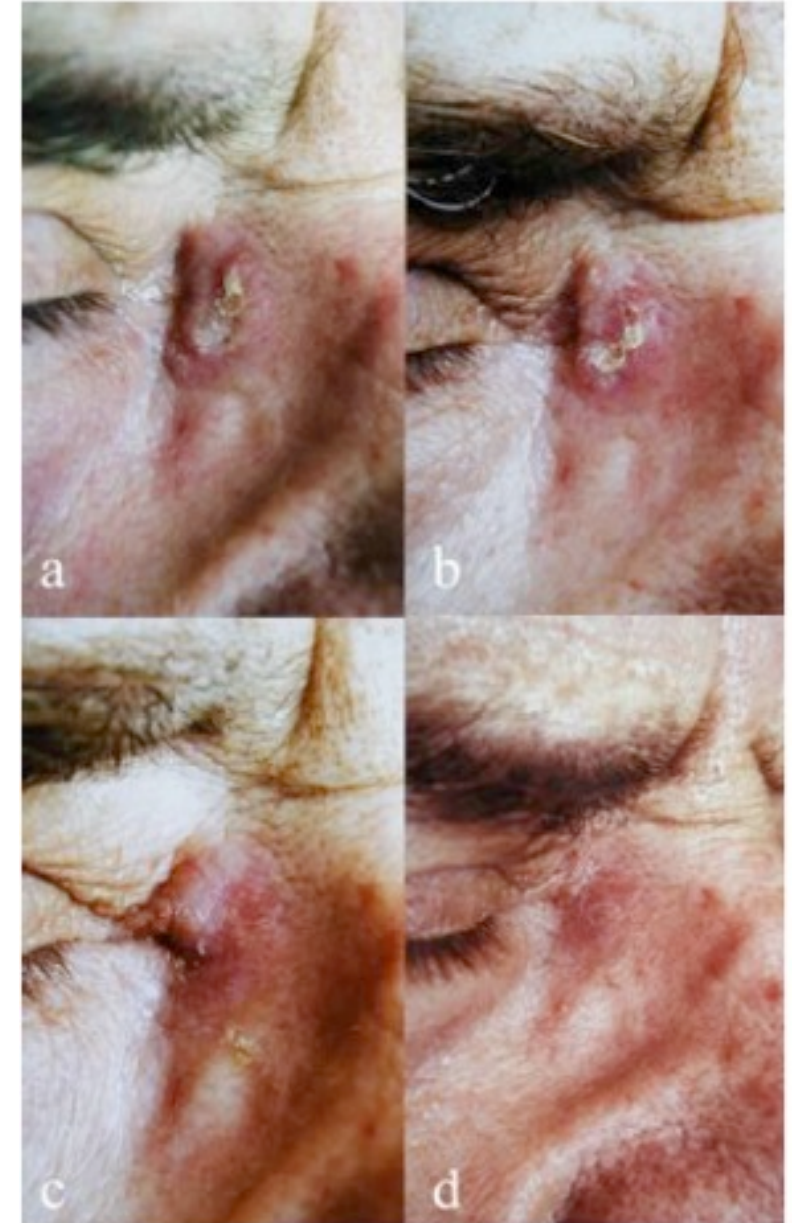


## Durable response of cutaneous squamous cell carcinoma following high-dose peri-lesional injections of *Viscum album* extracts – A case report

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## REVIEW

# Intratumoral immunotherapy: using the tumor as the remedy

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