Popperian Pathways: the demarcation between quack cancer cures and scientific remedies

Sir Karl Popper (1902–1994)

Michael Baum UCL November 2007
The Philosophy of Science:
THE OPEN SOCIETY
AND ITS ENEMIES
THE SPELL OF PLATO

To Michael from Karl
17-1-1943
Hospital; a wish to which they both were
adverse from the beginning...

I read your three offprints with great
interest. I agree that all biologist are, as
a matter of course, dualistic - but not "HOLISTS;"
and I formed your descriptions of which are
nice indeed; and I think - like you in your
Australian paper - that the Homoepaths are
"rationalists. I also think it very unlikely
that there are, or will be "alternative"
approaches of significance. But it is, of
course, most important that we never
know; and that science has often been pushed or
claimed from, the ideas of outsiders. (Both Kepler
and Newton used astrological ideas; and Galton,
who (rightly) disliked these ideas (wrongly) failed,
for this reason, to take Kepler seriously.) For this
reason, we ought to remain open-minded.

For me, the most interesting of your papers was "Limitations of Non-Science in Surgical Epistemology". I hope you may find time, one day, to discuss these issues with me.

Yours sincerely, Karl Potter
Inductive Logic

- Observations
- Hypothesis
- Corroborative Evidence
- Law of Nature
Logical asymmetry between verification and falsification

Swans are white

Or maybe black
If Herbalife truly enhances athletic performance then should it be classified like anabolic steroids?
Tectonic plate amulet to neutralize electromagnetic waves
NES Energetic Analysis done by an energy field scanner which shows up organs blocked by anything from environmental and nutritional chemicals to viruses.

“I’m sure that I need this machine to enable my body’s energy fields to re-align themselves and re-activate their innate self-healing abilities”.
Emotional Freedom Techniques (EFT) is a psychotherapeutic tool. The theory behind EFT is that negative emotions are caused by disturbances in the body's energy field and that tapping on the meridians while thinking of a negative emotion alters the body's energy field, restoring it to "balance."
Homeopathy

• The more dilute the evidence the more potent the effect!

• Homeopathy doesn’t poison your body, It poisons your mind
The Society of Homeopaths

HIV/AIDS Symposium
London: 1st December 2007

Join us at this one-day Symposium in London for a fascinating insight into the role of homeopathy in treating HIV/AIDS.

Our three expert speakers from a variety of backgrounds will present their experiences in the field, followed by ample opportunity for participants' questions and discussion during our "panel" session at the end of the day.

Jonathan Stalik, well known for his pioneering work with patients with HIV/AIDS and his book AIDS: The Homeopathic Challenge, will set the context for the day. His talk will introduce us to the unique role of homeopathy in the treatment of HIV/AIDS.

Mary Farquhar will tell us about the MUZ Homeopathy Project in Botswana, which she established in 1996. The project offers free homeopathy outreach to an area where over 50% of the people are infected with HIV or AIDS, one of the highest rates in the world. We will discuss the impact of AIDS in Africa using a new study of healing remedies created by Peter Chassart.

We anticipate that this thought-provoking day will generate much food for discussion and invite all participants to contribute their questions to the panel for the final session.

Jonathan Stalik

Jonathan Stalik was one of the pioneers of homeopathic treatment of HIV/AIDS at a time when there was widespread fear and ignorance of the disease both in society at large and within the medical profession. He worked for some 5 years at one of London's major centres for sufferers of the disease and despite the ever present challenges and threat of burn-out he helped many people. However, his pioneering work was overshadowed and discredited by the medical profession and practitioners, and his research was not acknowledged by the Society of Homeopaths. Later, his book, AIDS: The Homeopathic Challenge, led to demand for his further work around the world. At this Symposium Jonathan will talk about his fascinating experiences, set the context for the day and hopefully provide inspiration for those still on the road of discovery.
“The patient was given only 6 months to live but defied the doctor’s predictions, took snake oil daily and lived to a ripe old age”

This is an urban myth, there ain’t no such patients.
“The Patient was only given 6 months to live!”

“I don’t know why you wanted a second opinion.
Your doctor’s guess is as good as mine.”
The history of the treatment of breast cancer
The Edwin Smith Papyrus
The influence of Galen
200 CE-1840

Ah-ha, you need purgation, bleeding & leeches

Yuk!
Virchow  
1842  
Anatomical and Surgical Revolution
Halsted’s Hypothesis
The Agnew Clinic by Thomas Eakins
The Philosophy of Science:
Inductive Logic

Observations → Hypothesis → Dogma → Corroborative Evidence
Popper’s Pathways

Observations → Thesis → Experiments → Falsification

Observations → Anti-Thesis → Experiment → Falsification → Ad Infinitum

Revised Thesis
Inconsistencies in the Anatomical Model

• Impossible to define cure.
• It returns however perfectly it may be taken away.
• Lymph node metastases may occur in the absence of an obvious primary.
• Fisher’s mouse models.
“Radical surgery is like slamming the stable door after the horse has bolted”

“We see further because we sit on the shoulders of Giants”

?Isaac Newton
Conceptual Revolutions

“Paradigm shift”: Thomas Khun
Therapeutic consequences:

• Breast Conservation
Anatomical Model

Biological Model
Anatomic to Systemic

Breast cancer is a systemic disease.

Mastectomy vs. Lumpectomy

A U.S. study of breast cancer patients showed that there was no significant difference in survival between women treated with mastectomy and those treated with less extensive surgery.

Source: New England Journal of Medicine
Therapeutic consequences:

• Breast Conservation

• Adjuvant Systemic therapy
Adjuvant Systemic Therapy
Tamoxifen Chemotherapy

Anatomical Model

Biological Model
UNITED KINGDOM 1950–2002: Females
Breast cancer mortality at ages 20–49

*Mean of annual rates in component 5-year age groups

Source: WHO mortality & UN population estimates
UNITED KINGDOM 1950–2002: Females
Breast cancer mortality at ages 50–69

Death rate / 100,000 women, age standardised*

Source: WHO mortality & UN population estimates

*Mean of annual rates in component 3-year age groups
ENGLAND AND WALES 1950–2000: Females
Breast cancer mortality at ages 20–69

Death rate, age standardised

Year

Comparison of ATAC data with EBCTCG 1995
Overview¹: Hormone Receptor +ve Patients >50

![Graph showing estimated % still without recurrence as first event over years]

- Control (EBCTCG)
- Anastrozole (ATAC data)
- Tamoxifen (EBCTCG)
- Tamoxifen (ATAC data)

4-year recurrence-free rate:
- 92.2% (Anastrozole, ATAC data)
- 89.6% (Tamoxifen, ATAC data)
- 84.6% (Control, EBCTCG)

70.5% (Tamoxifen, EBCTCG)

¹EBCTCG. *The Lancet* 1998; 351: 1451–1467
Hmm, I think it's time for another paradigm shift
Clinical Inconsistencies in the Biological Model

• Anecdotal

• Distant metastases at the time of diagnosis.

• Hazard rates over time for metastases.
do occur, but they are exceedingly rare.

G. Penpineal recorded a case in which a woman, 50 years of age, had a small painless tumour in her left breast for twenty-two years. Then three months after an operation for removal of an adenoma of the ovary, the tumour of the breast began to grow rapidly. A year later it was excised and proved to be a Cancer. It recurred twice within the two following years.

In most of these cases, though the Adenoma and the Cancer are connected anatomically, it appears to be clear from examination after incision that the Cancer has not developed from the Adenoma. J. Hutchinson recorded a

1 Lectures on Surgery, 1829, p. 378.
2 Annales de Gynécologie, 1890, p. 35.
% dying within 2 years

% with metastases at presentation
Milan data in Disease-Free Survival format

Bonadonna, Valagussa et al. NEJM 1995
Annual distant recurrence (at known sites) rate among women given surgery but no or little radiotherapy (95% CI).

6789 events, 22,027 women, 195,757 pyrs.

Confidential: Not for citation or publication
Bimodal relapse pattern observed in mature Milan database (surgery only)

Months from surgery to first recurrence

Frequency
• Risk of recurrence peaks in the first 2-3 years following diagnosis\textsuperscript{1,2} and is associated with a poor prognosis\textsuperscript{3}.

\textsuperscript{2} Saphner T \textit{et al.} J Clin Oncol 1996; \textbf{14}: 2738-46.
Angiogenesis is Essential for Tumor Growth Beyond 1–2 mm\textsuperscript{3}, as well as for Metastasis\textsuperscript{1}

- Tumor growth regulated by a “switch” to a proangiogenic tumor microenvironment\textsuperscript{2,3}

\textsuperscript{1}Folkman. *J Natl Cancer Inst* 1990;82:4–6
\textsuperscript{2}Bergers, Benjamin. *Nat Rev Cancer* 2003;3:401–410
Ligand Binding

Receptor Activation

Pathway Activation

Gene Transcription

Proliferation/Maturation
Survival
Angiogenesis
Metastasis

Surgery and the new biology

Receptor
EGF
TGF-α
HRGs
BTC

Ligand Binding

Receptor Activation

Pathway Activation

Gene Transcription

Proliferation/Maturation
Survival
Angiogenesis
Metastasis

Surgery and the new biology
Angiostatin from primary tumour

Insulin like Growth Factor

Progesterone

TGF\(\beta\)

p53

Oestrogen

COX 2

Her 2

VEGF

Aromatase

TGF\(\alpha\)

Apoptotic Cells

Tumour Cells
Similarity of gene expression in fibroblasts in response to wounding to those active in Malignant disease.

“The way that tumours acquire the ability to create complex tissues does not involve their de novo invention of the complex programme of stromal activation. Instead they activate a latent pre-existing wound healing programme, that is encoded in the normal genome.”  

Weinberg, the Lancet
Hypothetical interpretation of Milan data base

- Induced angiogenesis: 10 months
- Induced cell division at surgery: 18-40 months
- Steady stochastic transitions. Natural history: 60-200 months
Does Breast Cancer Exist in a state of Chaos?
Baum & Chaplain European J Cancer 1999

DCIS
Both VEGFR and PDGFR Are Critical for Angiogenesis

In pre-clinical studies, sunitinib has been shown to inhibit both VEGFR and PDGFR.

Sunitinib Simultaneously Inhibits RTKs on Tumor Cells, Pericytes and Endothelial Cells

**Antiangiogenic effects**

- Cross-talk between PERICYTE, VASCULAR ENDOThelial CELL, and TUMOR CELL
- Inhibition of PDGFR, PDGF, KIT, VEGF, VEGFR-1, VEGFR-2, and VEGFR-3

**Antitumor effects**

- Inhibition of RTKs expressed by tumor cells
- Inhibition of PDGFRs

Multitargeted inhibition results in antiangiogenesis and reversal of tumor growth
New therapeutic windows

DCIS

sunitinib
"The fact is that one new idea leads to another, that to a third, and so on through the course of time until some one, with whom no one of these ideas was original, combines all together and produces what is justly called a new invention".

Thomas Jefferson
Traveller, there is no path; the path is made by walking”

Antonio Machado
I can now rejoice even in the falsification of a cherished theory, because even this is scientific success

John Carew Eccles
Nobel Lauriat for Physiology 1963
“It is not truisms that science unveils. Rather, it is part of the greatness and the beauty of science that we can learn, through our own critical investigations, that the world is utterly different from what we ever imagined-”

Popper  The Logic of scientific discovery