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EDUCATION AND DEBATE

A new homeopathic approach to neoplastic diseases: from cell destruction to carcinogen-induced apoptosis

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Neoplastic diseases are now among the most commonly seen conditions. Orthodox, non-surgical approaches, including chemotherapy and radiotherapy, have variable results, but many adverse affects that limit their use. These are sometimes the direct cause of death. More patients are choosing alternative treatments, mainly the homeopathic and herbal-nutrition approach.

Homeopathy does not have highly effective remedies for cancer in its literature, and has been limited to palliating the adverse effects of chemo/radiotherapy. Research into substances that can produce neoplastic diseases (carcinogens), may lead to them being used to treat the cancer they cause, according to the principle of similarity. I have used ultra-low doses (1×10^{-10} to 10^{-12} molar) of chemical carcinogens for 3–24 months, which have been given to cancer patients, usually in conjunction with conventional treatment. Using this procedure, complete remission or life extension has been achieved for some cancer cases. Three clinical cases are presented: a man with undifferentiated lung cancer; a child with an astrocytoma and a woman with leiomyosarcoma. *British Homeopathic Journal* (2000) **89,** 78–83.

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Introduction

After deaths due to cardiovascular and cerebrovascular disease, cancer is the most common non-communicable cause of deaths in adults.[1] The World Health Organization (WHO) estimates that in 2000, there will be over 10 million new cases of cancer diagnosed annually.[2] The costs and suffering due to neoplastic diseases are amongst the most expensive and exhausting of experiences for patients, their families and governments. An increase in the use of complementary and alternative medicine (CAM) for neoplastic diseases has been observed during the last 20 years; one in three cancer patients now use them.[3] The CAM therapies most used in cancer treatment are nutritional and herbal medicine, homeopathy, mind/body therapies and Iscador (mistletoe or Viscum album teraphy).

Cancer originates with a change in the structure of DNA. Transformation from a normal cell to a malignant cell depends on the mutation of genes that control cell cycle progression.[4] This usually involves an activation of oncogenes and/or down-regulation in tumour-suppressor gene function. Over fifty oncogenes are currently known to be involved in human cancers.[5] A point mutation, chromosomal translocation or gene amplification deregulate their expression or alter their structure, thus inducing production of a protein-signal implicated in cell cycle control. Usually such mutations induce cells to replicate their DNA and cause inappropriate survival/replication of cells.[6] One of the most common mutations found in cancer cells (at least 50% of all cancer types) is *p53*, a tumour suppressor gene.[7] If it is not present or not functioning, the cell will replicate continuously and become neoplastic. The types of point mutation in the *p53*

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gene vary depending on the type of cancer, suggesting that specific aetiologic agents are responsible for typical kinds and sites of mutations in the gene.[8]

Another class of genes thought to be involved in cancer are those involved in DNA repair and in maintaining genome integrity; their inactivation appears to facilitate mutations in oncogenes and tumour suppressor genes, leading to cellular proliferation.[5] These genes, together with tumour-suppressor genes, are usually considered to be involved.

Diagnostic procedures have progressed and advanced so far that it is now rare to miss the diagnosis of cancer when these methods are available. In terms of conventional treatment, surgical techniques cure many cancers. When the cancer type or stage is not amenable to surgical treatment, cancer cell destruction remains the cornerstone of regular treatment. Chemotherapy and radiotherapy try to eliminate the transformed cells through violent apoptosis,[9] but they do not correct the damaged genome; therefore the disease may recur. Chemotherapy has a low therapeutic index, because target receptors are present in both cancer and normal cells.[10] Chemotherapy and radiotherapy both produce many adverse effects, including second malignances.[11] Twenty of the most common drugs, including cancer drugs are definitely carcinogenic for humans, producing leukaemia, and bladder, cervical, vaginal breast and endometrial cancers.[11,12] These are the principal reasons why patients refuse or abandon conventional treatment. One different technique, genetic therapy, emerged in 1991 for malignant melanoma: the aim is not to kill cells, but to try to induce correction of a gene defect. Genetic therapy is growing fast, but problems finding safe and efficacious vectors, and very high costs, limit its use to high-tech research centres. Currently the real impact of genetic therapy is close to zero.[10]

Since deregulation control of the cell cycle is the essential distinction between cancer and normal cells,[13] it seems reasonable, as an ideal, to search for substances that could correct cell cycle control in cancer cells, rather than to try to kill them. As we have seen, mutations of cell cycle control genes drive cells to neoplastic transformation. So, why not try to correct these mutations and induce normal apoptosis in cancer cells? Why not try to downregulate expression of oncogenes? Why not try to upregulate tumour-suppressor and DNA repair genes? How can we do this? I think it may be possible to achieve this through biochemical modulation of the cell cycle control mechanism, with microdoses of carcinogenic substances used in homeopathic form. Use of carcinogens is based on the 'Similia Principle': A substance that produces a specific (artificial) disease in normal cells or organisms can cure the same disease when it presents spontaneously. Examples already used in therapy include: amphetamines or analogues in concentration/attention disorder, and thiazide diuretics in nephrogenic diabetes.

Why use carcinogens?

There is a lot of evidence to show that regulation of cell cycle control induces cytostatic (growth arrest) or cytotoxic (apoptosis) consequences in bacterial, animal and human cells, both normal and malignant.[14] This regulation normally functions through the *p53* and *pRb* genes. Mutation and/or loss of function of these genes permits cells to go into continuous and uncontrolled replication. The only known way to repair this loss or malfunction is genetic therapy, Through it has limitations in the availability of vectors, and cost. Recent evidence confirms the property of carcinogenic/genotoxic compounds (2-acetyaminofluorene, aflatoxin B1, *N*-ethyl-*N*-nitrosourea and *N*-methyl-*N*-nitrosoguanidine) to increase *p53* protein levels, which is capable of stopping replication of damaged DNA in cancerous cells.[15]

Other recent confirmation that genotoxic compounds are capable of inducing incomplete differentiation, apoptosis and degradation of oncogenic protein in cancer cells,[16] comes from the successful use of arsenic trioxide (an old homeopathic remedy and potent carcinogen and leukaemogenic substance) in acute promyeloycytic leukaemia (APL).[17] The mechanisms are downregulation of the *bcl-2* gene[18] (an oncogene) and degradation of oncogenic promyelocytic leukemia/retinoic acid receptor (PML/RAR) protein.[19] Arsenic is effective only for APL and not for other types of leukaemia.[20] The dose is in the range 5–10 mg daily for two to four weeks. No major side effects were seen.[21] This evidence shows that gene regulation, and the consequent apoptosis, can be caused by some substances, including a carcinogen compound.

Another possible and synergistic mechanism for tumour-cell regression is the correction of genetic damage through the use of DNA-repair enzymes (endonucleases, alkyltransferases and methyltransferases). These enzymes are a security mechanism to prevent replication of damaged DNA; they stop replication at cell cycle checkpoints. Mutations that impair the ability of cells to recover from DNA damage can enhance the spontaneous mutation rate and lead to cancer.[22] Loss of *p53* and DNA-repair enzyme genes cause cells to lose the ability to stop cell replication at checkpoints.[23] Induction of hepatic alkyltransferase can be achieved in animals by a hepatic carcinogen, 2-acetaminofluorene (2-AAF), as long as two weeks after a single dose of 60 mg/kg.[24] Other alkyltransferase inducers are partial hepatectomy, X-ray irradiation, and bleomycin.[25] Even alkyltransferase induction seems to be regulated in animals by the *p53* gene function.[26]

Induction of endonucleases can be achieved in bacterial cells by superoxides (superoxide-dysmutase),[27] in human breast cancer cells by hormones and analogues,[28] and in rat hepatocytes by secondary nitroalkanes such as 2-nitrobutane and 3-nitropentane, which are powerful carcinogens in the rat liver.[29]

Methyltransferase induction can be achieved by using ionizing radiation in rat cells.[30] The protective, antimutagenic and antineoplastic effect of X- rays in animals and cells exposed to the methylating/carcinogenic agents *N*-methyl-*N*-nitro-nitrosoguanidine[31] and *N*-ethyl-*N*-nitrosourea[32] has been demonstrated; So why not use it in the inverse sense? Induction of DNA repair in cancer cells with small doses of methylating or alkylating agents seems logical. At the moment, the potential role of DNA-repair enzyme induction as a target in conventional cancer treatment has not been investigated. Of particular interest is the observation that human breast epithelial cells, transformed by chemical carcinogens *in vitro*, express genomic changes similar to those found in spontaneous breast carcinomas.[33] Why not utilize this carcinogen's specific tropism for genetic material, and use it in the inverse sense?

Of course this is not the first report of the double property of carcinogens to produce both cell proliferation (neoplasia) and cell destruction (apoptosis); Melzer,[34] in 1980, summarize an ample literature showing that carcinogens induce cell death or growth inhibition, both *in vivo* and *in vitro*. Hooson and Grasso,[35] in 1977, tested 20 chemical carcinogens and found depressed growth and division of cultures in rat kidney cells. Zhu,[36] in 1991, describes how the colon carcinogen dimethylhydrazine produces micronuclei and apoptosis in rat colon cells. A simple metal carcinogen, hexavalent chromium, shows the same property in hamster ovary cells.[37] The potent hepatic carcinogen, 2-acetaminofluorene, induces both proliferation and apoptosis in rat biliary epithelial cells.[38]

Is it ethical to use a carcinogen to treat cancer patients?

Many carcinogenic compounds are widely present in general life: a long list of colour or flavour food additives are in daily use, and are listed as carcinogens by the National Toxicology Program and the International Agency for Research on Cancer.[39] Iodine 131 (^{131}I) is used to treat hyperthyroidism, and is associated with colonic and gastric cancers.[40] Many conventional medicines are inducers or promoters of malignances,[11,41] and all these substances are used in higher doses than those I use in treatment. The doses I use are below those recommended by the Environmental Protection Agency (EPA).

Professor Benjamin Bonavida at the University of California at Los Angeles (UCLA), has shown pro-apoptotic action with very low doses of toxic substances such as Tumour Necrosis Factor (TNF) and subtoxic concentrations of adriamycin/cisplatinum in resistant human ovarian cancer cells.[42] His work shows how minimal concentrations of toxic substances can induce gene regulation.

Clinical cases

Three clinical cases from my private practice are presented; all three consulted me for alternative or complementary options due to their desperate condition following opinions from well-qualified oncologists. Carcinogenic substances are used as homeopathic remedies at concentrations between 1×10^{-9} to 10^{-12} molar, equivalent to a 9- to 12- decimal dilution. Due the lack of pharmacopoeial method for working with these substances, I prepared them according to their molecular weight, or molar concentration: for example; 3, 4-benzo(*a*)pyrene has a molecular weight of 252.3, thus 252 mg in 1 L of ethanol or 1 kg of lactose will be the mother tincture or mother trituration. It was triturated in lactose to the 4th decimal, one hour for every step and then potentized in 87% pharmaceutical ethanol, to the 12th decimal potency with 100 succussions at every step. The medicine was given orally, impregnated on sugar pills at the 9th to 12th decimal potency.

The first patient is a 48-year-old man, who in July 1998 accidentally discovered a large right supraclavicular node: biopsy showed a non-differentiated lung carcinoma. The primary tumour was a non-surgical 2.5 cm mass in his upper right lung, biopsed by needle. A lesion in the sternum was observed on isotope bone scan. Due to his poor prognosis he decided try homeopathic medicine. The treatment included classical medicines to ease chemo/radiotherapy side effects, and a 1×10^{-9} molar (9x potency) of benzopyrene (one of the most powerful lung carcinogens). After three months with this combined treatment, a second lymph node biopsy showed fibrous tissue, and at the fourth month an upper right lobectomy was performed showing only fibrous tissue in a 2 cm scar. No neoplastic cells were seen. At this time the sternal bone lesion remained unchanged, and two oncologists suggested that it was not cancer related.

Five months later, a sharp pain on the patient's right thorax wall led to a repeat bone scan. This showed multiple metastases in the thoracic wall, arms and skull. It seems that the open lobectomy broke the delicate balance and led to a relapse. In August 1999, 15 months after diagnosis, the patient was alive, but in a very poor condition.

The second patient is a 5-year-old boy who developed bilateral strabismus (abnormal alignment of both eyes) in February 1993. An ophthalmologist recommended a CT scan which showed a brainstem tumour, probably an astrocytoma, measuring $39\times19\times21$ mm. Two weeks later, an open craniotomy was performed with 60% tumour excision. The pathologist reported a grade II astrocytoma; Dr Epstein and his team at New York University reported a grade III astrocytoma. Subsequent chemo/radiotherapy failed to stop tumour growth. After three months, when he finished his chemo/radiotherapy treatment, and with a worsening neurological condition, his parents decided to try homeopathic treatment. After six months of daily administration of two nitrogenated purine and pirimidine bases—nitrated guanine ($guanine_3-NO_3$) and nitrated xanthine ($xanthine_3-NO_3$) at 1×10^{-6} molar

or 6x potency—tumour growth ceased. Twenty-four months after the beginning of treatment, NMR showed no tumour and his neurological condition was back to normal. Forty-five months later, he is completely asymptomatic. In August 1999, the child again developed bilateral strabismus. A repeat NMR scan revealed a recurrent brainstem tumour measuring 6×4 cm. Two neurosurgeons agreed that it was inoperable. With combined conventional chemotherapy (Temozolamide) and homeopathic treatment (*Arsenicum album* 6x and nitrated *Guanidine* 6x) for six weeks, the tumour reduced in size to 2×2 cm, against all expectations (Figures 1–3).

The third patient is a 43-year-old woman who, in 1995, had a hysterectomy for carcinoma of the corpus uteri. Three years later, sudden onset of dyspnoea lead to a chest X-ray. Eighty percent of her lungs were affected by uncountable metastases. A needle transthoracic biopsy showed a leiomyosarcoma. Six months of platinol-based chemotherapy produced some reduction in the number of metastases, but she had to stop treatment due to thrombocytopaenia. In March 1998 she started combined treatment with daily methyl-cholantrene 1×10^{-10} molar, or 10x potency. Every month, chest X-rays have shown improvement, finally reducing the number of shadows to 10–15% of the original count. Her clinical condition was perfect in August 1999. The oncologist's opinion is that the remaining shadows in the lung fields are due to scarring (Figures 4 and 5).

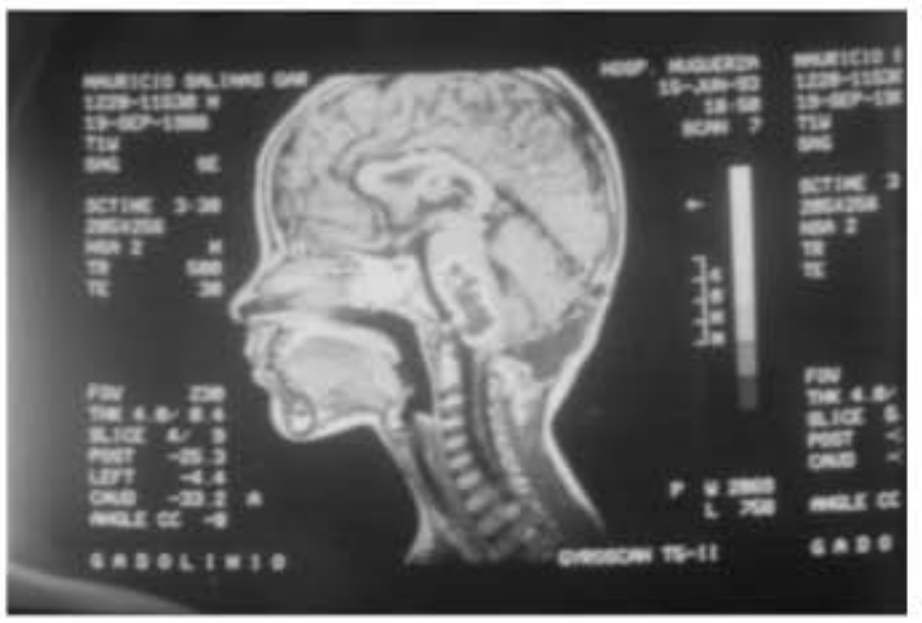

Figure 1 Case 2: CT scan June 1993: Beginning of homeopathic treatment: 42 mm diameter tumour.

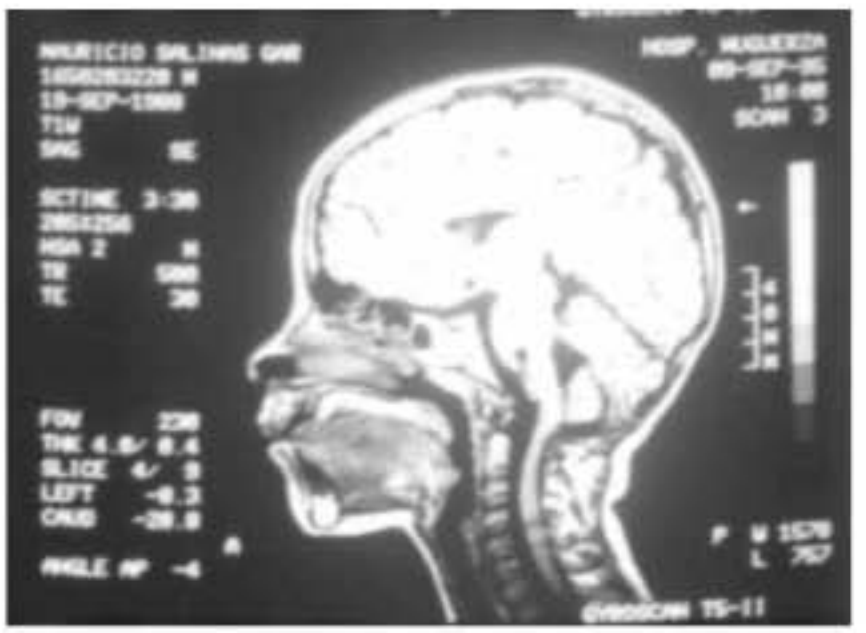

Figure 2 Case 2: CT scan September 1995: After 24 months of homeopathic treatment: no tumour visible.

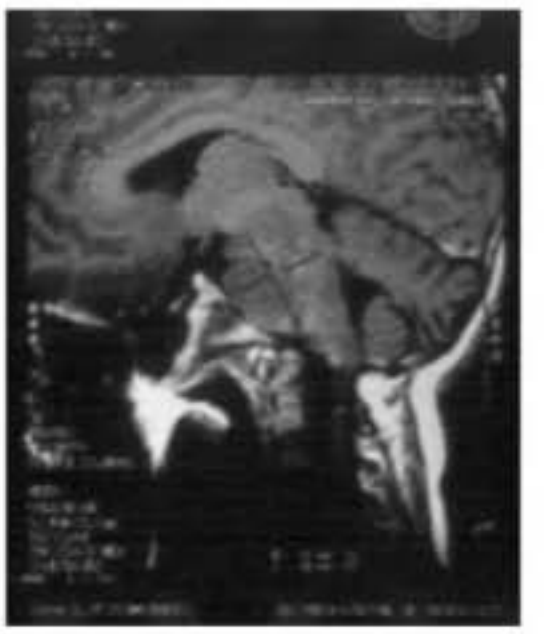

Figure 3 Case 2: NMRR scan September 1999: After 47 months recurrence of tumour at same location: 31 mm maximum diameter. the mass reached 60×44 m in December 1999, and reduced to 20×20 mm in January 2000.

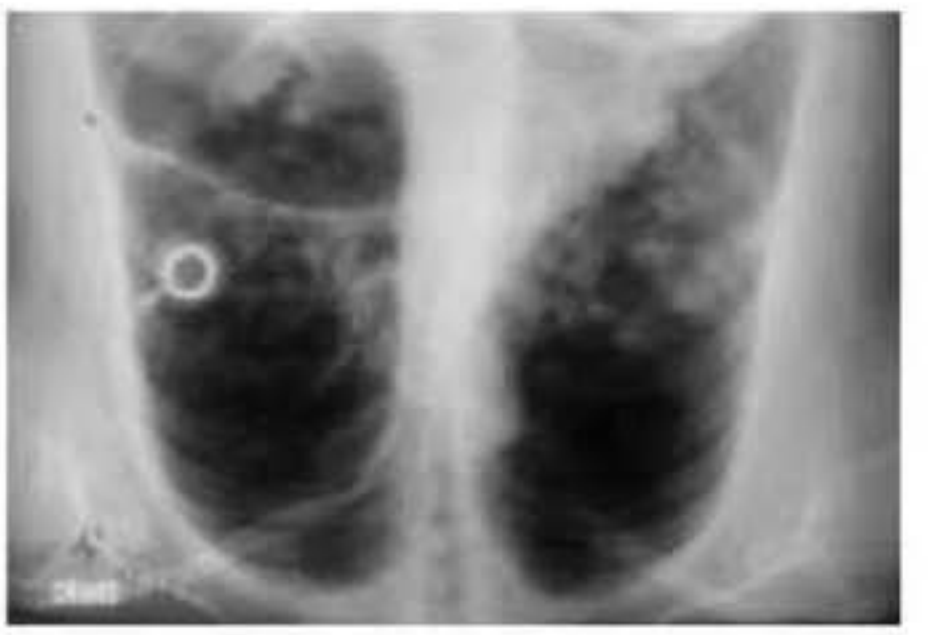

Figure 4 Case 3: X Ray chest April 1998: At beginning homeopathic treatment, uncountable leiomyosarcoma metastases in lung fields.

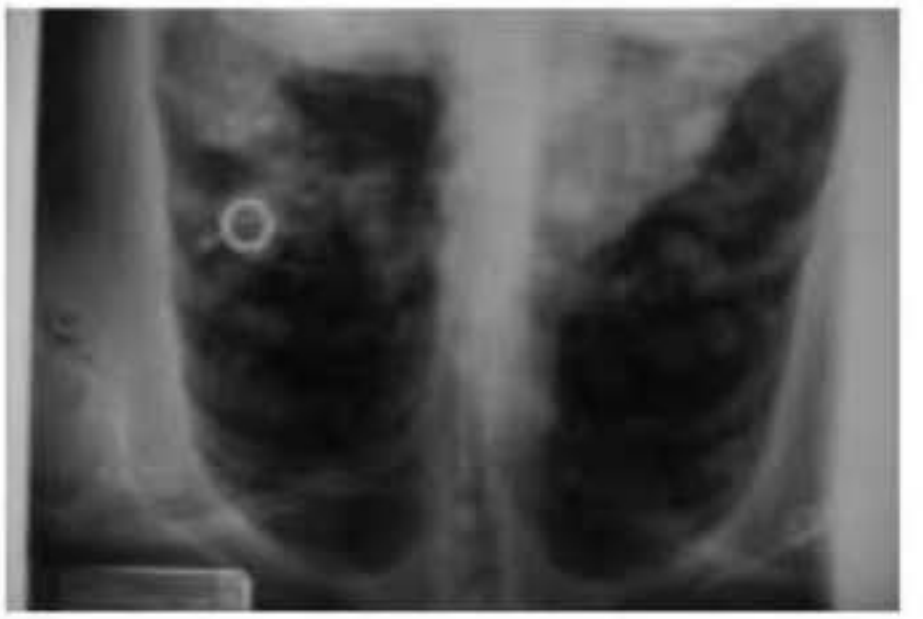

Figure 5 Case 3: X Ray chest March 1999: After 12 months of homeopathic treatment: reduction in number and size of metastases, bullae at right lung base.

Conclusion

Beside some anecdotal and poorly documented references to cancer cures with homeopathic treatment, this is the first documented approach to the treatment of neoplastic conditions using the Principle of Similarity. No side effects due to homeopathic treatment were seen (second malignancies, toxicity).

The promise of molecular oncology exists;[43] perhaps this new homeopathic approach will open doors to that era without having to wait for another 25 years or more.

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