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SPONTANEOUS OR INDUCED REGRESSION OF CANCER A NOVEL RESEARCH STRATEGY FOR AYURVIDYA

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***ABSTRACT** : Regression of cancer has been an interiguiny factor for medicinal science. This article is bringing out some interesting data on this issue with a view to generate in the Ayurvedic researchers to see the possibilities of Ayurveda in induced regression of cancer.*

Indeed, if a phenomenon appears just once in a certain aspect, we are justified in holding that, in the same conditions; it must always appear in the same way. If, then, it differs in behavior, the conditions must be different…..". I said, indeed, that we must never neglect anything in our observation of fact, and I consider it indispensable.. Nothing is accidental, and what seems to us accident is only an unknown fact whose explanation may furnish the occasion for a more or less important discovery".

Claude Bernard[1].

A sudden disappearance or a massive regression of cancer has been well documented, in the medical literature, for more than a century. According to the Catholic Church records, St. Peregrine was spontaneously cured of his leg cancer, after his intense faithful prayers. He lived a fruitful life upto 80 years and died in the year 1346 A.D[2]. He was canonized as the patron saint of cancer and malignant diseases. In India, two great saints Bhagwan Sri Ramakrishna Paramhansa and Sri Ramana Maharsi died of laryngeal cancer and sarcoma respectively. They are our patron saints. Sir William Osier, in 1901, published a paper entitled, "The Medical Aspects of Carcinoma of the Breast, with a Note on the Spontaneous Disappearance of Secondary Growths"[3]. In conclusion, Osler stated that the phenomena observed, "are among the most remarkable which we witness in the practice of medicine, and the truth of the statement that no condition, however desperate, is quit hopeless". Such well-documented regressions of cancer are "whispers of nature" which we must listen more closely and with a total absorption. Then there is a chance that we may be able to follow Claude Bernard's instructions to understand and create the very conditions which led to the natural regression of cancer. This is the research trail we have followed for many years. It was on 20th April 1966 that one of the authors (ABV) noted down, in his journal, a hypothesis to explain the regressions due to A.C.S.-an anticancer substance[4]. How the principles and practices in Ayurveda can dovetail into this hypothesis is the partial story that we would love to share with all of you. That path emerges in Ayurvidya-Ayurveda and Life Sciences.

In the manuscript of Bhrigu-Samhita, cancer has been described and, to Maharsi

Bhrigu, Shukracharya has expressed, **"etadSasya ih icaik%saa vaOva/ Nasya ih. Baarto jaayato dova. SauBaarMBaao ip vaa Bavaot\. tdahM BaartM (anyaM manyao naa~ihsaMSaya:..**" ODeva! If therapy for such a lesion (cancer) is discovered in India or even a beginning is made then I'll doubtlessly consider Bharat to be a blessed nation. "This aspect was covered in the M.D. Dissertation of one of the authors (ABV), "The Medical Aspects of Bhrigu – Samhita". Even certain remedies were described for cancer in the manuscript of Bhrigu-Samhita[5]. The remedies described were Ashwagandharishta, Yogarajguggulu, Vasantkusumakar Rasa, Ganges water, Heerak Bhasma, auto-urine therapy etc. In Agastya Nadi Reading, at Chennai, the following prescription for cancer was successfully employed in a woman with metastatic cancer: Crocus sativus, Shorea robusta, Pongamia pinnata, Eclipta alba, Centella asiatica, Lippia nodiflora and Papaver somniferum. The women then had cancer regression and lived for two years more[6].

A leading surgeon, Tilden C. Eversen from the University Illinois College of Medicine, reported that over 1000 cases of spontaneous of cancer were known in literature, in 1964[7]. The number has steadily increased over the last four decades, with a better documentation. Eversen chose to analyse 130 cases, which had a robust histopathologic and clinical documentation. Over 50% of these 130 were represented by four types of cancer: (1) neuroblstoma, (2_hypernephroma (3) choriocarcinoma and (4) malignant melanoma. Eversen, after studying the conditions in each case, suggested the following as putatively responsible for the regression: (1) Hormonal withdrawal, (2) Unusual response to usually inadequate therapy, (3) Fever or acute infections (4) Allergic and immune reactions (5) Removal of the carcinogenic agent (6) Interference with the nutrition of the cancer (7) Complete surgical removal and (8) Incorrect histological diagnosis. This was a bold but too broad an attempt. Hence there were few takes of the hypotheses for further research. But the review clearly established that the host response-immunological or other dose exist in the biological control of cancer. The immunology of cancer got a major boost[8]. But the practical consequences were not commensurate with the basic research efforts. However, certain major advances have already been made.

While several heroic attempts have been made to cure cancer, one of the landmark discovery has been the work of William B.Coley. He devoted a lifetime to understand how infections can cause partial or temporary regressions of cancer. He induced erysipelas and succeeded in getting complete regressions in some patients with sarcoma etc[9]. But the obstacles were immense, as therapy itself was quite hazardous. One would strongly recommend to all cancer-scientists, the review of the influence of bacterial infections and of bacterial products (Coley's toxins) on malignant tumors in man[10]. One of the authors-H.C. Nauts, 23 years later, reported another case of metastatic melanoma, in whom intralesional injections of bacterial toxins led to a regression and the patient was clinically well 5 ½ years after he had lung metastates[11]. The further work on bacterial lipopolysaccharides and the induction of fever, proinflammatory cytokines and enhanced immune responses has vindicated the pioneering work of William B.Coley, an unsung hero of medicine.

Jwara in Ayurveda, is considered Rog-Raj-the king of all diseases. Jwara is not merely a rise in the body temperature-pyrexia[12]. The current research on the molecular mechanisms of fever has more than vindicated the Ayurvedic experience and treatises on Jwara. Bacterial lipopolysaccharides (LPS) induces several pro inflammatory cytokines-Tumour-necrosing factor (TNF - α), Interleukin (IL-1 β), interferon γ ect[13]. These cytokines do activate tumour-killing. Recently, monoclonal antibodies that blocked TGF beta and TL-10 receptors led to tumour rejection in mice, infected with Friend Leukemia virus. So the steps in the management of Jwara do also become very relevant to tumour regression. Immunotherapy of cancer has to consider the basic understanding of Jwara, in Ayurveda, to attain a grater degree of success. Antitumour effects of challenging antigens were demonstrated when the responses were associated with hypersensitivity to the agents. Hence mast cells, eosinophils, IGE etc, besides killer T cells, do play a role in cancer regression[14]. Dendritic cells loaded with tumour antigens led to regression of malignant melanoma in patients. Ayurvedic udvartan may have immune enhancing activity.

A shift in the paradigm can be made by incorporating the correlation of the ancient insights into Jwara and the modern discoveries in the molecular mechanisms of fever. This approach may open up a novel understanding of the pathogenesis, Progression and management of cancer. We have to learn how periodically moderate fever may enhance the host immunological surveillance against the cancer cells[15]. May be the over-use of antibiotics and antipyretics, for even a mild fever, may negatively influence the host-control of the transformed cells. Recorded cases of regression of cancer after fever or infections do suggest a need to look in this direction[16]. The fact that TNF- γ, IFN γ, apoptosis-inducers etc. do have a role in cancer cell death, emphasizes this research path. In Ayurvidya, we have to address this question at multiple levels of biological organization-from a cancer cell line to metastatic cancer in man. We have to reassess Cooley's approach with state of-the -art Ayurvidya (Life Sciences + Ayurveda)[17]. Not only controlled induction of fever but appropriate attention to Brinhan and Langhana is essential, as per the individual cancer patient's status. Fasting has been shown to benefit in reducing the tumour growth in animals and regressions have been reported, in cancer patients, after fasting. “Big eaters” have been stated to be prone to cancer, particularly with a larger intake of salt[18].

But it is equally desirable to investigate the regressions reportedly induced by Ayurvedic or herbal remedies. There has been a massive screening of medicinal plants and herbs for anticancer activity viz. Cytotoxic properties. The vinca alkaloids of Catharanthas roseus, taxol from Taxus baccata, camptothecins, podophyllotoxins etc have evolved as drugs[19]. But the screening of Ayurvedic remedies / Plants to enhance the immune surveillance by the host, to prevent carcinogenesis or to regress the metastates have not been encouraged much by the funding agencies. It is interesting to note that as early as in 1925, K.K. Chatterji, a surgeon from Calcutta, published in The Lancet some dramatic regressions of cancer with the Neem oil and copper salts of margosic acid[20]. He had also studied ethyl esters of various oils for his studies. He said, “In some cases treatment with ethyl esters, copper margosate has cleared up the growth and removed all evidence of malignancy”. The injections were also given locally in

the tumour mass. Chatterji did refer to the properties of Neem, in Ayurveda. Table 1 lists some of the Ayurvedic plants which show promise for a team effort of research to induce cancer prevention, relief and regression. The approach has to take the Reverse Pharmacology Path - starting from Ayurvedic experience that is well -documented[21]. We have to move from experience to exploratory studies and then to well-designed experiments-basis and applied.

The most interesting and challenging aspect for research in Ayurvidya is the presence of anticancer substances in the urine, shown by the Nobel Laureate Albert Szent-Gyorgyi[22]. Ashtamutra and their properties have been quite well-described in Ayurveda[23]. John W. Armstrong published a book, "The Water of Life", in 1944[24]. He had combined fasting (Langhana), with local and systemic use of autourine. The dramatic results obtained in some cases of gangrene emboldened him to study the effects of auto-urine therapy in patients with cancer. He has reported several cases of breast cancer responding to fasting and auto-urine therapy. Subsequently in India, Sri Morarji Desai and Dr. Paragi desai popularized auto-urine therapy during the last century[25]. All this would have remained only in the fringe medicine but for the case-studies and experiments cited below.

Mackay cited a case of regression in breast cancer with metastatic pleural effusion and ascites[26]. She could not swallow even liquids and starved. The pleural and the peritoneal fluid got absorbed and the tumours regressed dramatically. While publishing the case, Mackay gave an interesting title, "A case that seems to suggest a clue to the possible solution of the cancer problem". It is proposed by us that the putative anti-cancer substance sequestered in the malignant fluids, reached a critical plasma and tissue level on reabsorption of the fluids. This probably led to apoptosis of the malignant cells. Novak, in 1960, showed regression of metastases and primary tumours in several cases after injection of ether extract of urine[27]. He also published the X rays showing regression of metastases. However, our hypothesis of anti-cancer substance in human urine emerged because Cole had reported that urinary bladder cancers spontaneously regressed in several patients after ureterosigmoidostomy. One of us (ABV) had proposed that A.C.S. extracted in the urine, after ureteric implantation in the sigmoid, got absorbed from the colon and reached critical plasma levels to eventually induce the regression through triggering a cascade of vascular, allergic and apoptotic events. To reinforce this hypothesis, we came across a case of spontaneous regression at Yale Medical School, Mrs. Elizabeth Morrow (Unit No. 71-42-56) was admitted and operated partially for abdominal wall leiomyosarcoma in 1960. She underwent another operation for her stress incontinence. She developed vesicovaginal fistula, which could not be repaired despite several surgical attempts. Finally when her fistula was repaired, she presented with metastases, in 1967. So the six long years her tumour stayed regressed (suppressed) apparently due to a continuous absorption of ACS from her vagina, due to the fistula. We have come across another case-report of leimysarcoma, this time of the bladder. Bladder was resected and the ureters were reimplanted. For six years, there was no recurrence[28]. This was ascribed to better prognosis in children. But it could be that A.C.S. played a role.

In the Year, 1947, Williams and

Walthers had shown inhibition of tumours with the extracts of urine[29]. In 1963, Szent-Gyorgyi et al proposed in "Science" a possible new approach to cancer therapy. They detected in human children's urine, two natural substances which they termed retine (for retarding cancer) and promine (for promoting cancer). In mice, solid Krebs 2 ascites tumour were transplanted behind the scapula. Daily subcutaneous injection of retine, in 0.1 ml of peanut oil, were given for 10 days. Retine tended to stop the further growth of the tumours and could make cancer, already developed, regress. In a further study with adult human urine, they could confirm the results with retine[22]. However, all their efforts to isolated and characterize retine have failed[30]. Sarkar et al had shown an inhibitory effect on DMBA- induced mammary tumours in Holtzman rat, from India, with human urinary extract[31]. They ascribed it to LH-like fraction. In India several cases of cancer regression have seen anecdotally reported[32,33]. However, a systematic experiential study with cow's urine has been recently initiated at Bhavan's SPARC and some other centers.

We had started observing cancer patients, who themselves opted for autourine therapy, way back in 1966. In a male patient (RJ), with cervical metastases, auto-urine therapy for 31 days led to a 65% reduction in size of the lymphnodes, which became soft. However, the patient was lost to follow-up but on enquiry death was reported within a year. Another female patient (RB), had ovarian cancer diagnosed in 1992. She was a very well documented case (Tata BJ 15570, HN 9252744). She was operated twise, given a full course of cancer chemotherapy, radiation etc. But she developed metastases and malignant ascites. There was no response to the continued treatment. She then used to fast often. She started taking her urine five times in a day and also had urine packs on her body. She had continued autourine, three times in a day, for seven years. She took 5-7 small pieces of Tinospora cordifolia and prepared tea-like extract, which she took instead of water and continued for 2 ½ years. She had totally changed her food habits and took figs, vegetables, soup, mung and chapatti. Her ascites disappeared and the metastases regressed completely. When we saw her, it was seven years after the first definitive diagnosis.

We now understand that it is very difficult to conduct clinical therapeutic research in cancer patients by non-cancer investigators. But if a team and collaborative approach is evolved for exploring the role of Ayurvedic modalities-plants, Gomutra, Pathya etc- there is a chance that we may successfully apply the insights gained from spontaneous regression for control of malignancy. Then we may all realize that often cancer is a chronic disease and needs longterm care through life-style changes, dietary care and biological modalities to enhance host control of tumours. From Asadhya roga we may move to Kashtasadhyata and eventually sadhyata. Ayurveda would have a major global impact even if we partially succeed.

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Table 1
Ayurvedic plants and formulations with anticancer potential

Ayurvedic plant	Activity	Ayurvedic formulation	Activity
Azadirachta indica	Vranghna, Richikara	Vasanta kusumakarrasa	Rasayana
Ocimum sanctum	Deepaniya, Adaptogen	Yogarjguggulu	Multiple effects
Tinospora cordifolia	Rasayana, GM-CSF	Arogyawardhani	Pittahara, Ruchikara
Curcuma longa	Vranapaha, Antimutagen	Arbudahararasa	Rasayana
Semicarpus anacardium	Vahnikar, Varanahara	Heerakbhasma	Rasayana
Withania somnifera	Rasayana, Kshayapaha	Gomutraghanavati	Multiple actions
Commiphora wightii	Deepaniya, Receptors	Triphala	Rasayana, Vranahara
Pongamia pinnata	Vranahara, Immunity	Sudarshanaghanavati	Immunostimulant
Butea frondosa	Sheetal, Rasayana	Vijayadi choorna	Vedanahara, Pachani
Ficus racemosa	Vranashodhana, Hima	Dashamoola kwath	Multiple effects
Allium cepa	Balya, Rochana	Vidangadi choorna	Krimighna, Jwarahara
Shorea robusta	Vranashodhana, Vishaha	Sarivadi vati	Tridoshaghna