In the Multipronged approach to CANCER... The latest weapon is

AiET

In technical collaboration with
Biotherapy Institute of Japan, Tokyo, Japan.

Autologous Immune Enhancement Therapy

A treatment using the patient's own immune cells, to fight & control Cancer.

For the first time in South Asia by

Nichi-In Centre *for* Regenerative Medicine
NCRM
Visions & Hope. Immortal.

Nichi-In Centre
for
Regenerative Medicine.

In Association with

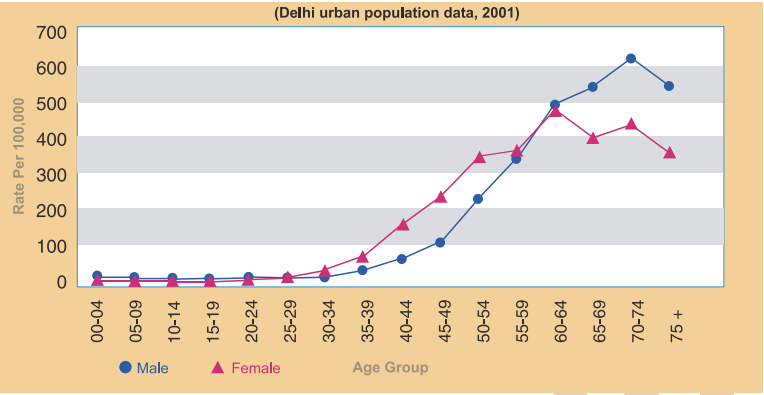
nichi vision
LIFESCIENCES
www.nvls.in

http://www.immunotreatment.org

Introduction

Despite numerous advances in medicine, Cancer remains a major health problem. It is the second leading cause of death in the world, yet much is still not known about its mechanisms of development and definitive modalities of complete cure. Globally it is estimated that there are 7.6 million new cancer cases, of which 52% occur in developing countries every year. The magnitude of the problem of cancer in the Indian sub-continent in terms of sheer number is most alarming. The estimated new cases of cancer in India per year is nearly 6.5 lakhs (1999) and at the start of the millennium it was estimated to be 806,000. The crude incidence of cancer in India is approximately 100 per 100,000 population. Cancer in women in the Indian sub-continent constitutes more than 50% of the total incidence. Recent epidemiological studies done at National Cancer Registry programme in India report that Cancer burden in the country is 2.5 to 3 millions and estimated number of new cases diagnosed every year found to be around 800,000 [1].

Indian Scenario of Age Specific Incidence of all Cancers



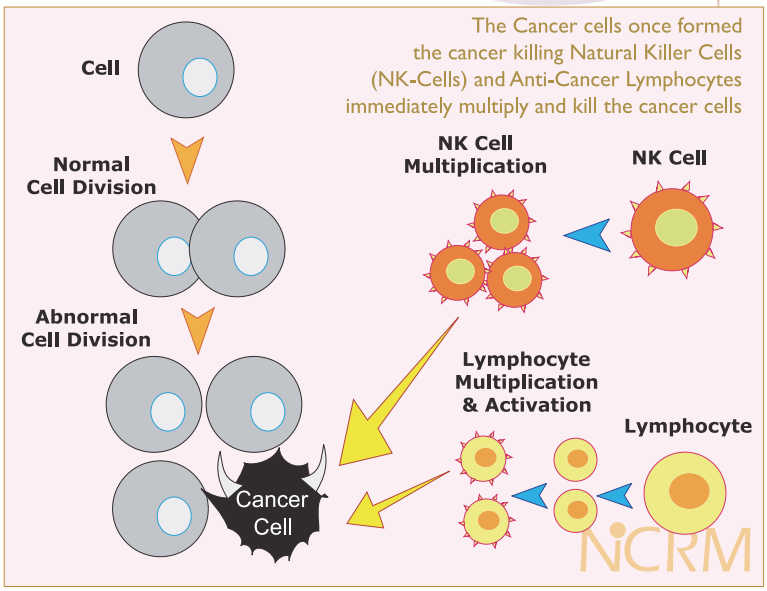
Data Source: Cancer Incidence And Mortality in Delhi UT Urban; Delhi Cancer Registry, Dr BRAIRC Hospital, AIIMS, 2006.

Although the common treatment modalities such as surgery and/or chemo and radiotherapies have been playing major roles in bringing down the mortality and morbidity to a significant extent, complete cure is still uncertain and the prognosis varies depending upon the stage and the type of the disease. Even when patients experience tumor regression immediately after therapy, recurrence or metastasis (spreading to other parts of the body) can occur later.

Immune system & Cancer: Almost everyday several cancer cells are formed in our body. This is because thousands of cell divisions take place in the body every day and a few of such divisions resulting in mutated cells result in the birth of a cancer cell (or cells), which are killed by the body's immune system. The immune system is a complex network of cells and organs comprising of Lymphocytes, Macrophages, Dentritic cells, Natural Killer cells (NK Cell), Cytotoxic T Lymphocytes (CTL), Lymph nodes etc.., that work together to defend the body against attacks by "foreign" or "non-self" invaders including cancer cells. Immediately upon a cancer cell is recognized, the Lymphocytes get activated and engulf the same and/or the NK cells attack the cancer cell to kill it (Fig.1). When the immune system's efficacy is overwhelmed by the cancer formation abundantly, or when the immune system is weaker, then cancer evolves as a full blown disease and starts growing.

Cancer cells are formed everyday in our body. They are immediately killed by the body's Immune system.

Bodys Immune Mechanism against Cancer Prevention

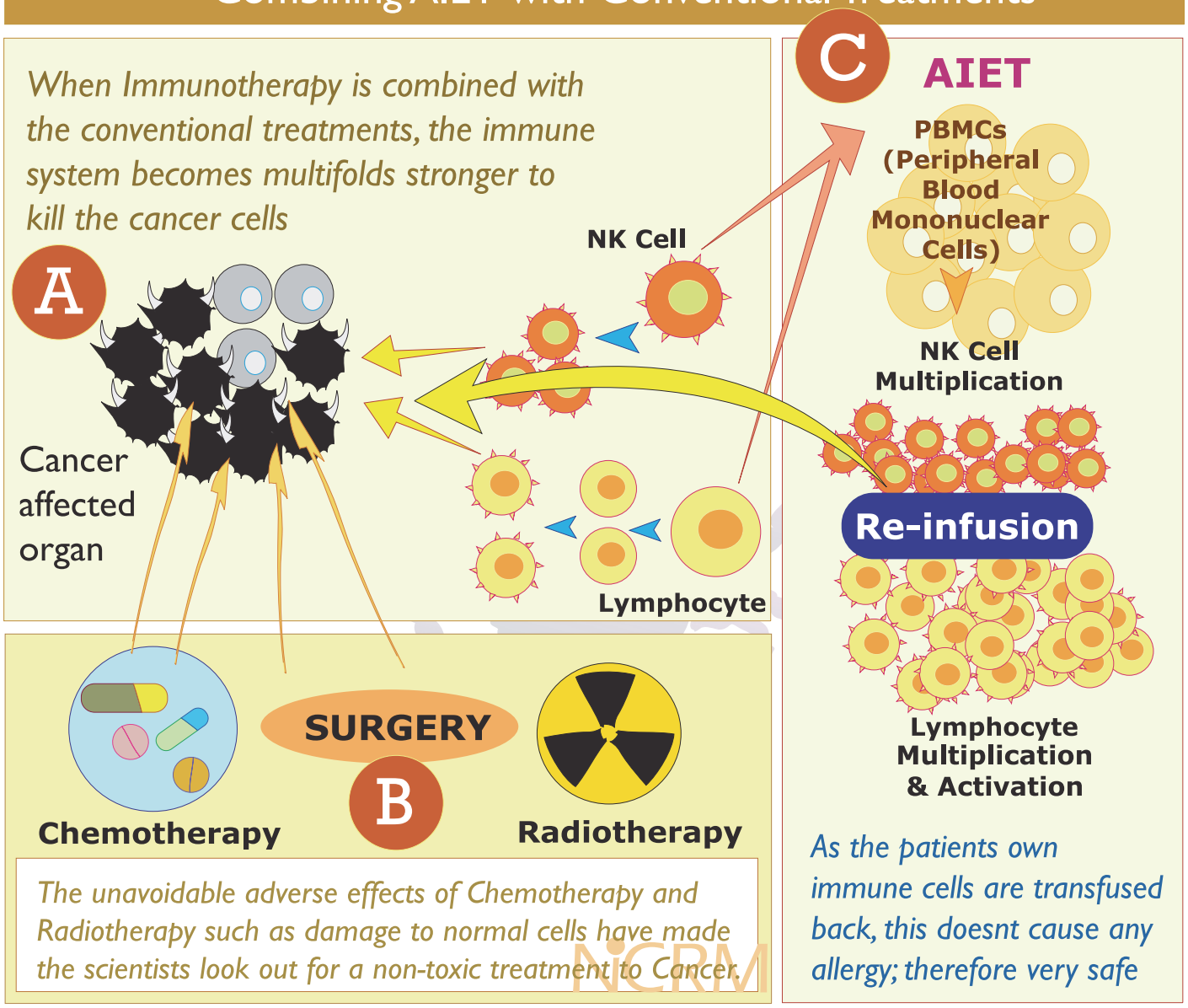


Given the variable nature of cancerous cells, each cancer behaves somewhat unique. In general, a multi-pronged approach to cancer is vital as cancer grows at different rates and respond to different treatments and people with each specific cancer need specific combination of treatment aimed at their particular kind of cancer. When the spread of cancer is very deep, total removal of the cancer growth by surgery may not be possible. At times, after removing a portion of the cancer, radiotherapy and/or chemo-therapy may be necessary to treat the remnant portion of cancer.

It has been widely recognized that Chemotherapy of cancer has profound toxic side effects and has certain limitations in efficacy. Radiotherapy is also a very effective mode of treatment in certain types of cancer, but with its own adverse effects as well. These two modalities affect not only the cancer affected cells, but also the normal cells (Fig.2-B).

Multi-Pronged Approach: As there is no single fool-proof methodology of treatment for cancer, a multi-pronged approch is essential. In the multi-pronged approach to treat cancer, the latest scientific advancement has yielded Immune therapy and cancer vaccines as well. Consequently, many patients with advanced cancer opt for less toxic therapies like immuno cell therapy and cancer vaccine which are collectively known as Biological therapy. Immuno Cell therapy is a promising new addition to the family of cancer treatments that includes surgery, chemotherapy, radiotherapy and cancer vaccines. This mode of treatment uses the body's immune system, either directly or indirectly, to fight cancer by enhancing the immune mechanisms of the body. As this therapy uses only the patients own cells for treatment, it is very safe and doesn't result in any allergy and combining this (Fig. 2-C) with the conventional therapy(ies) appropriately asper the patients condition, type of cancer and regimen of chemo/radio therapies, improves the outcome. As the immune cells of the patient upon transfusion doesn't affect the normal functioning cells of the body, it is furthermore safe.

Combining AIET with Conventional Treatments



A. When body's immune system is unable to control the multiplying cancer cells, it becomes a full blown disease.

B. The available treatments give relief, though not total, depending upon the extent of the disease, but have their cytotoxic side efffects.

C. When Immunotherapy is combined with the present treatments, it enhances the body's immune system multi-fold to fight cancer, with almost no side effects .

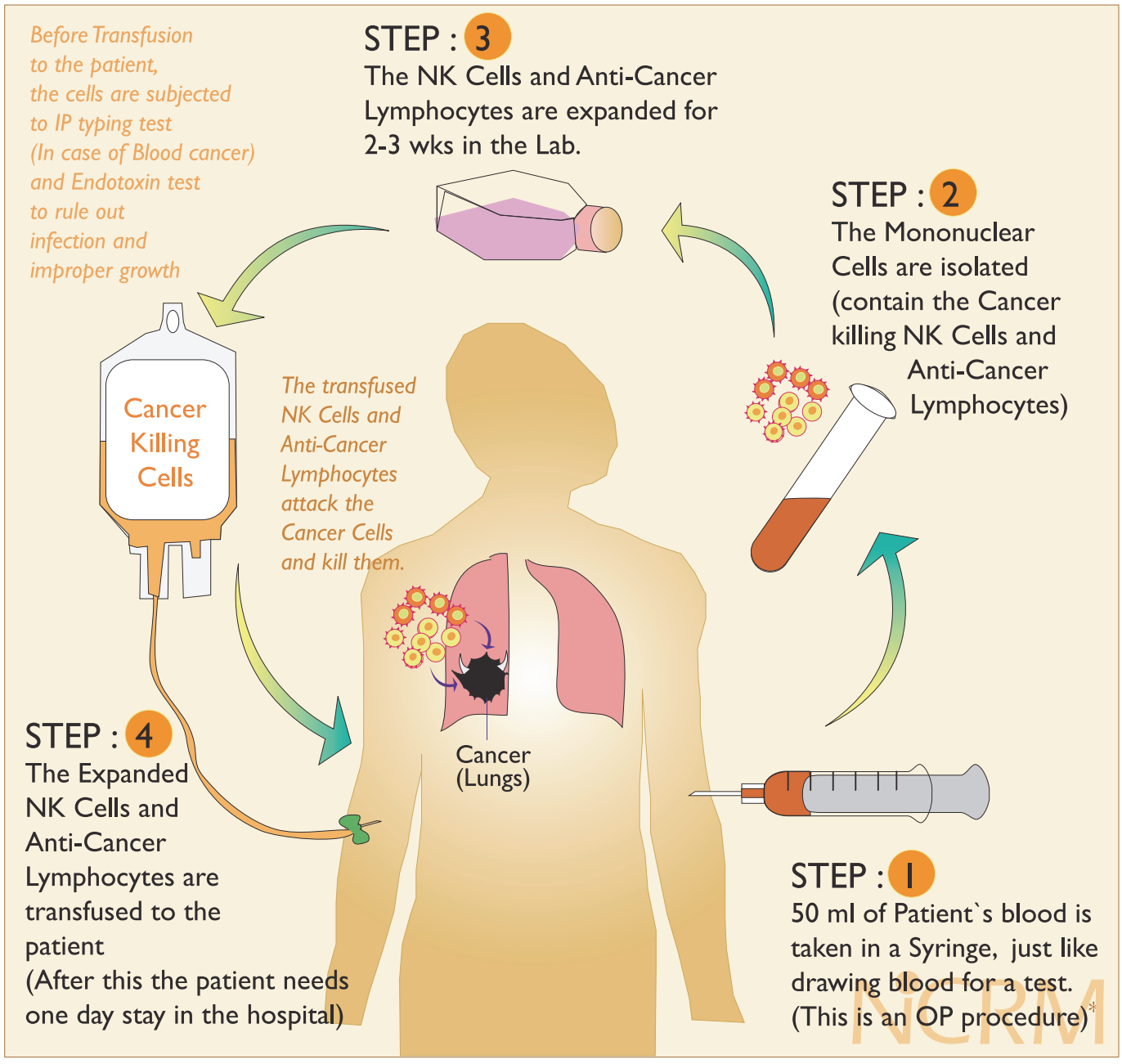
Origin of Immunotherapy:

For most of the 20th century there was no concrete evidence that human cancer antigens existed or that there were any measurable immune responses against growing cancers in patients. A major development in this field was the identification of the antitumor properties of Interleukin-2 (IL-2), a cytokine produced by helper T lymphocytes that is a major regulator of immune reactions [2].

The interaction of antigens with T lymphocytes activates lymphoid cells to express receptors for IL-2, and the simultaneous stimulation of IL-2 secretion leads to the expansion of immune cells and effective immunity. Research done by Dudley and colleagues at the National Institute of Health USA, demonstrated that antitumor impact of administration of IL-2 is a result of stimulating immune reactions in vivo.

Autologous Immune Enhancement Therapy (AIET) has a successful clinical history in Japan, Europe and USA for the past two decades. Immuno cell therapy of cancer using autologous lymphocytes activated in the laboratory was first introduced by Rosenberg et al., of National Institute of Health USA. In the late 80s, they published a turning-point article in which they reported a low tumor regression rate (2.6~3.3%) in 1,205 patients with metastatic cancer who had undergone different types of active specific immunotherapy (ASI), and suggest AIET kind of immunotherapy combined with specific chemotherapy as the future of cancer therapy [3].

Stepwise procedures involved in the AIET



**Unless the patients general condition warrants, the patient can go home after STEP I and needs hospital visit for STEP4 after 2-3 wks*

AIET is a treatment method in which some immune cells are taken out of a patient's own *(Autologous)* peripheral blood or bone marrow **(Step:1)** from which Mononuclear cells are isolated **(Step:2)** which are then cultured and processed to be activated or to acquire additional functions **(Step:3)** until their resistance to cancer cells is strengthened and the cells are put back in the body **(Step:4)**.

There are three requirements for an effective immunotherapy for cancer such as (i) A sufficient number of appropriate tumor reactive lymphocytes *(cancer fighting cells)* must be present in the peripheral blood of the patient (ii) Lymphocytes

must be capable of reaching and extravasating at the site of the cancer and (iii) Lymphocytes at the tumor site must have appropriate effector mechanisms to destroy cancer cells. Blood or bone marrow from a donor *(allogenic)* may also be used. Since patients own cells have less chance of rejection compared with the of a donor, it is proven that autologous cells are much safer than allogeneic donor.

Dr. Terunuma (sitting, Right) with his colleagues

Immune enhancement therapy has a lot of hope to cancer patients, as enormous potentials of our body's immune system which we have been exploring only in the last decade have yielded impressive results in our experience of nearly 10000 patients -Dr. Hiroshi Terunuma.

AIET in India - NCRM Experience : It was in 1999 when the first private clinic in Japan with a cell processing facility and specializing in immuno-cell therapy was established. Dr. Hiroshi Terunuma heads the Biotherapy Institute of Japan (BIJ) which treats almost 10-20 patients every day with an overall efficacy of this treatment when added to the conventional treatment more than 20-30 % [4-7]. BIJ apart from offering AIET, has been exploring in depth the finer components of innate immunity against cancer in the form of Cytotoxic T lymphocytes, γδ T cells (gamma delta T cells). NCRM, having signed a collaborative agreement with BIJ is the first and only Institute in India to provide this AIET involving NK Cells and CTLs for patients with Cancer. NCRM's technology uses only the patient's own plasma for the procedure of cell culture of NK cells and CTLs and it doesn't employ any feeder layers used in techniques elsewhere which makes the procedure much safer [8]. In India, till date 40 patients with different types of cancers at various stages have been administered AIET by NCRM.

The progress in the development of Immunotherapy for the treatment of patients with cancer is growing at a rapid pace. The promise for the future of this exciting and evolving field is much anticipated.

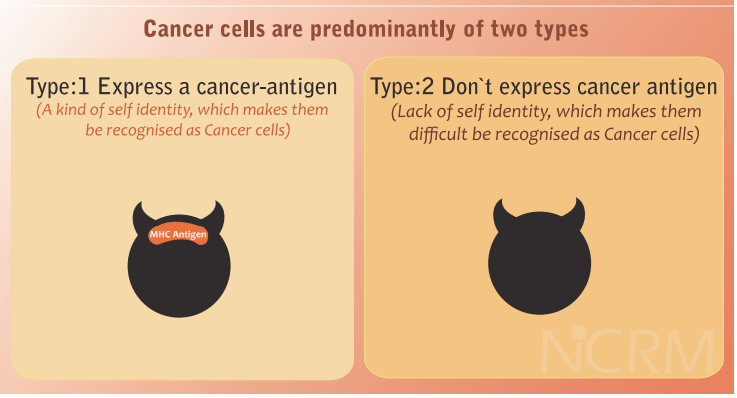
S.A Rosenberg
NATURE
Clinical Practice Oncology
March 2003; No.2; Vol 3; 115.

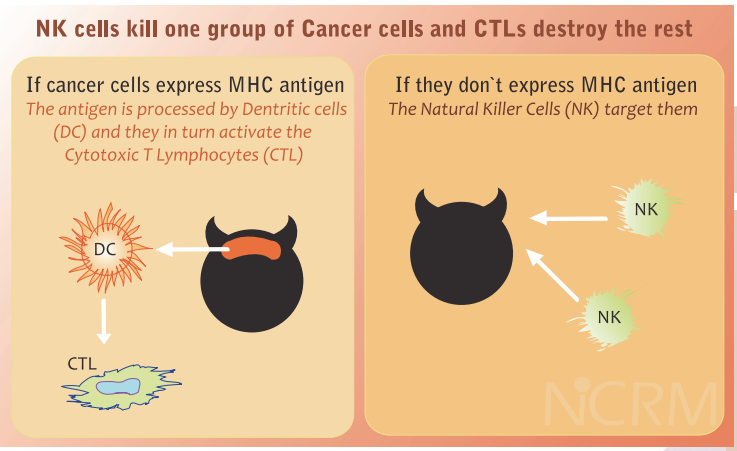
To mention a few, A male patient aged 40 years with Stage III (advanced) adenocarcinoma of the pancreas was given three transfusions of expanded NK and Cytotoxic T Lymphocytes along with surgery and adjuvant chemotherapy by NCRM. There was considerable improvement in the quality of life of the patient after the first transfusion. The patient subsequently underwent two more transfusions of AIET and improved with a significant tumor response proven by a steady decrease in tumour marker CA 19-9 values from 3800 to 750 and a tumour progression-free survival beyond 24 months [9].

A 54 years old female diagnosed with papillary serous cystedeno-carcinoma of Ovary with lymph node metastasis, lesions in the liver and spleen (stage III-C) was given four cycles of AIET along with Chemotherapy. The CA-125 cancer marker before the therapy was 243 U/Ml. After three cycles of AIET, the PET-CT images showed marked regression of lesions in the spleen, stable hepatic lesions and decrease in size of the inguinal lymph nodes with no recurrence in the pelvic region. After another three cycles of AIET, the CA-125 came down to 4.7 U/ml. The patient reported improvement in appetite and quality of life with no adverse reactions [10].

Further details on the types of cancers treated till date in India can be found at http://www.immunotreatment.org/casereport.htm

Our advantage : The NK cell + CTL combination





Advantages of AIET

The presently available and widely used treatments for cancer include conventional approaches such as chemotherapy, radiotherapy and surgery. Each have their own limitations and side effects. AIET is the least toxic of all these therapies [11]. The Immunotherapy is the most natural of present treatments available for cancer and since it strengthens the body's immune system it can even decrease the side effects of other cancer treatments which are used along with Immunotherapy.

It has been observed that when cell based immunotherapy is combined with conventional treatments, the efficacy improves by 20-30% [12] and less than 1% of the patients experienced fever or a rash making this treatment is free of significant side effects when compared with other standard cancer therapies.

In AIET the Natural Killer (NK) cells and Cytotoxic T Lymphocytes (CTLs) from the patient themselves are directly activated, expanded in the lab and when reinfused back to the patient they can effectively act against the tumour cells .The unique feature of AIET provided by NCRM is that this therapy involves infusion of activated NK cells and CTLs which can target both type of cancer cells, those that express the MHC class I molecules and those that do not. Cells which express MHC class I are destroyed by the CTLs while those that do not are killed by the NK cells thus bringing an efficient destruction of the cancer cells .

The recent shot-in-the–arm for AIET is the finding that the Cancer stem cells are preferentially killed by NK cells [13, 14] and the T cells [15, 16]. With these evidences it is appropriate to say that AIET apart from destroying the tumour would benefit the patient by destroying the circulating cancer stem cells also thereby preventing metastases and recurrence.

Another added advantage is AIET can be administered for brain tumours also. Contrary to the notion that Immune cell therapy might not be effective in brain tumours, as immune cells cannot cross the Blood Brain Barrier, recent evidences have demonstrated the infiltration of Immune cells particularly the cytotoxic T lymphocytes into the brain .Immunotherapy has been shown to be effective against high grade malignant brain tumours including Glioblastoma [17].

AIET for Wellness

Studies have proven that the NK cell profile of cancer victims is significantly lower than their peers without cancer [18, 19]. On another perspective the antigen sensing of Viruses and cancer cells by the NK cells is by similar mechanisms. Evidences are piling up that the NK cells and CTLs which are the major weapons used in AIET against cancer are also effective against viruses such as HIV, Hepatitis C, Influenza, and Epstein Barr Virus(EBV). Thus individuals with lower immunity, those susceptible to cancer and viral infections, those under stress, those with diagnosis of chronic fatigue syndrome and those suffering from above mentioned viral infections can undergo Autologous immune Enhancement therapy (AIET) in addition to the other therapies they are undergoing such as antiviral therapies and supplementary therapies to enhance their immunity for effective response against the diseases and also as a preventive strategy.

Limitations of AIET

A major limitation to the development of effective immune cell based therapies for patients with cancer has been the inability to mediate the prolonged persistence of the transferred cells. A study demonstrated that there was a significant correlation between tumor regression and the degree of persistence in peripheral blood of adoptively transferred T cell clones, suggesting that inadequate T cell persistence may represent a major factor limiting responses to AIET [20].

Moreover the "immune-evading" nature of the cancer cells which is enhanced by the "tumour microenvironments" poses a major challenge and is the prime area for future research on targeting the cancer cells in such tumour microenvironments which are very unique.

References

1. Vinod R, Tyagi BB, Manoharan N., Cancer incidence and mortality in Delhi UT urban - 2001 (Publication by Delhi Cancer Registry, Dr BR Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences)
2. Yang Q, Hokland ME, Bryant JL, Zhang Y, Nannmark U, Watkins SC, Goldfarb RH, Herberman RB, Basse PH, "Tumor-localization by adoptively transferred, interleukin-2-activated NK cells leads to destruction of well-established lung metastases", Int J Cancer. 2003
3. Rosenberg SA. Adoptive immunotherapy of cancer: accomplishments and prospects. Cancer Treat Rep. 1984.
4. Takada M, Terunuma H, Deng X, Dewan MZ, Saji S, Kuroi K, Yamamoto N, Toi M. Refractory lung metastasis from breast cancer treated with multidisciplinary therapy including an immunological approach. Breast Cancer. 2010 Mar 31
5. Hiroshi Terunuma, Xuewen Deng et al. Adoptive immunotherapy of cancer with ex vivo expanded, Autologous NK cells. The Society for Natural Immunity 2005; 9th Meeting, NK Hawaii B070.
6. Dewan MZ, Takada M, Terunuma H, Deng X, Ahmed S, Yamamoto N, Toi M. Natural killer activity of peripheral-blood mononuclear cells in breast cancer patients. Biomed Pharmacother. 2009
7. Dewan MZ, Terunuma H, Toi M, Tanaka Y, Katano H, Deng X, Abe H, Nakasone T, Mori N, Sata T, Yamamoto N. Potential role of natural killer cells in controlling growth and infiltration of AIDS-associated primary effusion lymphoma cells. Cancer Sci. 2006.
8. Abraham S, Manjunath S, Senthilkumar R, Murugan P, Srinivasan V, Thamaraikannan P, Tholcopiyan L, Srinivasan T, Preethy SP, Dedeepiya V, Terunuma H. Ex vivo expansion of clinical grade Natural Killer cells without feeder layers in stage III-IV cancer patients, post-chemotherapy and radiation. Cancer Immunotherapy and Immunomonitoring (CITIM) Conference; Budapest, Hungary; May2-5, 2011.
9. Sivaraman G, Pandian A,Baskar S, Senthil KR, Senthilnagarajan R, Dedeepiya V, Abraham S.Autologous Immune Enhancement therapy for advanced carcinoma of pancreas a case report.PASRM, III annual symposium 2008
10. Abraham S, Ramanan G, Dedeepiya V, Manjunath S, Senthilkumar R, Murugan P, Srinivasan V, Thamaraikannan P, Tholcopiyan L, Srinivasan T, Preethy SP, Baskar S, Terunuma H. NK cell-based autologous immune enhancement therapy for advanced carcinoma of ovary – a case report. Cancer Immunotherapy and Immunomonitoring (CITIM) Conference; Budapest, Hungary; May2-5, 2011.
11. Kohji Egawa. Immuno-cell therapy of Cancer in Japan. Anti Cancer Res 2004
12. Shigenori Goto, Noriko Shirotani et al. Clinical Benefit of Nontoxic Therapy in patients with advanced cancer. Anti cancer Res 2002.
13. Tseng HC, Arasteh A, Paranjpe A, Teruel A, Yang W, Behel A, Alva JA, Walter G, Head C, Ishikawa TO, Herschman HR, Cacalano N, Pyle AD, Park NH, Jewett A. Increased lysis of stem cells but not their differentiated cells by natural killer cells; de-differentiation or reprogramming activates NK cells. PLoS One. 2010.
14. Castriconi R, Daga A, Dondero A, Zona G, Poliani PL, Melotti A, Griffero F, Marubbi D, Spaziante R, Bellora F, Moretta L, Moretta A, Corte G, Bottino C. NK cells recognize and kill human glioblastoma cells with stem cell-like properties. J Immunol. 2009.
15. Weng D, Song B, Durfee J, Sugiyama V, Wu Z, Koido S, Calderwood SK, Gong J. Induction of cytotoxic T lymphocytes against ovarian cancer-initiating cells. Int J Cancer. 2010 Dec 10.
16. Ahmed N, Salsman VS, Kew Y, Shaffer D, Powell S, Zhang YJ, Grossman RG, Heslop HE, Gottschalk S. HER2-specific T cells target primary glioblastoma stem cells and induce regression of autologous experimental tumors. Clin Cancer Res. 2010 .
17. Sasaki K, Zhu X, Vasquez C, Nishimura F, Dusak JE, Huang J, Fujita M, Wesa A, Potter DM, Walker PR, Storkus WJ, Okada H. Preferential expression of very late antigen-4 on type 1 CTL cells plays a critical role in trafficking into central nervous system tumors. Cancer Res. 2007.
18. Imai K, Matsuyama S, Miyake S, Suga K, Nakachi K.Natural cytotoxic activity of peripheral-blood lymphocytes and cancer incidence an 11-year follow-up study of a general population.Lancet. 2000
19. Montelli TC, Peracoli MT, Gabarra RC, Soares AM, Kurokawa CS, "Familial Cancer:depressed NK-cell cytotoxicity in healthy and cancer affected members", Arq Neurosiquiatr 2001.
20. Rosenberg SA, Dudley ME. Cancer regression in patients with metastatic melanoma after the transfer of autologous antitumor lymphocytes. Proc Natl Acad Sci U S A. 2004

This brochure gives only a basic outline of the immunotherapy and its benefits as well as other points of importance & relevance, based on publications cited as reference.

This may be referred only as a general information and for specific needs of such treatment, each patient's condition will have to be analysed by a qualified oncologist and decided upon further, as immunotherapy alone is not a single standard therapy for cancer and may have to be combied with any one of more of the conventional treatments for cancer such as Surgery, Chemotherapy & Radiotherapy.

For private circulation only

For further details, contact:
Nichi-In Centre for Regenerative Medicine (NCRM)
PB 2278, Chennai 600026, TN, India
Tel +91 44 42321322, 24816743; ncrm@nichimail.jp

NCRM HAS STARTED CHANGING LIVES...

...ADDING SMILES TO FACES & VALUES TO LIFE

YOU TOO CAN BE A PART OF THIS MISSION

Hope foundation is a public charitable trust helping research & development activities, in health care especially for cancer. You too can be a part of this mission by helping us to add smiles to faces and values to life.

Donations are exempted from Income tax 80(G).

For further details contact us at: hope@hopefoundation.in

Thanks to

HOPE FOUNDATION

hopefoundation.in

for their support

FREQUENTLY ASKED QUESTIONS

1. Can AIET be used for all cancers?

Yes it is applicable for all cancers in general. But very good results have been reported with Renal Cell cancer (Kidney), Malignant Melanoma (Skin), Advanced Pancreatic Tumors, Lymphomas, Breast Cancer, Ovarian Cancer, Liver Cancer, Lung cancer, Colon Cancer, cancer of Esophagus and some types of Leukemias (Blood cancers). Terminally ill patients with metastases in the Lungs, Liver and Bone have also been treated with AIET.

2. Can AIET be given for haematological malignancies (Blood Cancers)?

Yes, AIET has been given for haematological malignancies like AML, ALL etc. Since in haematological malignancies the blood component themselves are cancerous, enough precautions are to be taken to ensure that the cancerous blood cells don't grow or overgrow in the culture though it is very unlikely as in our studies the NK cells have been found to destroy such cancerous cells during the culture process itself However, to ensure further safety of the AIET transfusion additional IP typing marker studies are performed to check that there are no cancerous cells in the AIET transfusion

3. What are the procedures involved with immunotherapy?

a) Blood is collected by a simple puncture of the vein as is done for any other lab test.

b) The collected blood is then processed in the specialized lab by specially trained scientists under highly sterile and aseptic techniques.

c) The application of the proven Japanese technique (Technical Collaboration M/S Biotherapy Institute of Japan) in the culture of the cells will result in three events. i. Activation of Lymphocytes ii. Expansion of natural killer cells, iii. Multiplication of Cytotoxic T Lymphocytes

d) After the process is completed the cultured cells of the patient are transfused (Given Back) to the patients as an intravenous drip some 10-20 days after the blood was collected from him/her.

Since the growth of the cells is controlled by multiple factors, the exact date of the transfusion will be known only after the cells start growing in the lab. The NCRM staff will be in touch with your treating physician to intimate to you well in advance about the exact date/day of the transfusion.

Please note that additional quantity of blood may have to be collected from the patient in between the transfusions of AIET for the purpose of obtaining autologous serum for cell culture

4. What are all problems that are anticipated during the administration of the cells?

In general there are no major adverse effects because the patients are given back the cells that were originally collected from them. Therefore the infusion is well tolerated. But during the process of destruction of the cancer cells by the cultured cells that are transfused, the patient may experience fever/fatigue on the day of administration. The risk of this is however is small. It occurred in less than 1% of patients in a study population that included more than 1400 patients.

5. Can the AIET be taken simultaneously with chemo or radiotherapies?

YES. AIET can be given with chemotherapy and/or radiotherapy. Since chemotherapy will reduce the peripheral blood count, we recommend the patient to start the AIET even before the start of chemo for better NK cell and CTL efficacy. The transfusion can be given in between chemo cycles in coordination with the oncologist. For the best results, before 3 days of the AIET transfusion, the chemotherapy should be stopped and resumed 3 days after the AIET transfusion.

6. Can the AIET be taken along with other kinds of alternative cancer therapies?

As long as the alternative therapy is not cytotoxic it can be taken simultaneously with AIET

7. Are there any situaions where blood cannot be harvested for AIET?

AIET involves the multiplication of NK cells and CTLs which are taken from the patient's peripheral blood. Therefore unless patient has normal or near normal values of peripheral blood cell count, the outcome of the cell expansion might not be optimal. Usually in patients who have undergone chemotherapy, the peripheral blood count could be low.

8. Are there any diseases/conditions in which AIET is contraindicated?

Since AIET involves autologous immune cells, this may not be indicated in patients who have auto immune diseases (such as SLE etc). In addition those patients under any form of immunosuppressive therapy should inform us in advance to plan the timing of the transfusions

9. What precautions does NCRM take during the culture?

The culture technique is sterile so as to ensure that no bacterial contamination takes place. This is also objectively tested by 'Endotoxin test'. If it is negative it implies that there is no bacterial contamination and only then will the cultured cells be administered to the patients.

10. How do you know that the right type of cells have been multiplied?

The cells after harvesting from the patient will be subjected to IPT (Immunophenotyping) by using flow cytometry. Then again after the process of expansion is over, the cultured cells will once again be subjected to IPT to check the quantity and quality of the desired cells before administering to the patients. This is done by a third party organization and the reports will be sent to the treating physician.

11. What is the success rate?

As in the treatment of cancers by other conventional methods, the patients who come early do better. A study which compared patients who have undergone the conventional treatment alone (Group 1) with that of the patients who have undergone the Immunotherapy in addition to the conventional treatment (Group 2) a 25-35% better results were obtained in Group 2 patients.

12. What are the Dosage requirements and timing of administration?

The dose is determined on a case to case basis. If the cancer is solid and has been removed completely by surgery 2 transfusions may be sufficient while 4 –6 Transfusions are required if the patients is receiving chemotherapy after surgery. 4 –6 Transfusions are required for blood malignancies.

13. What is the basis on which, the number of cycles of AIET transfusion are decided?

This is based on earlier studies and experience and the severity of the disease of the individual patient. As the patient might be undergoing or have undergone other treatments such as surgery or chemotherapy or radiotherapy, the remaining cancer in the body is adjudged by taking into account, the tumor size and tumor markers where relevant. So until the tumour markers become lesser gradually or until the tumour starts either shrinking or comes to a static non-progressive status, we have to keep treating it. In the first 2 or 4 cycles of AIET if there are positive signs of such improvement, then further cycles could be given more aggressively.

14. How do you follow up the patients after AIET is done?

Depending upon the severity of the cancer, we recommend several cycles of AIET Transfusions. After atleast 3 to 6 weeks of transfusion the patients can be followed up by analysing the tumor markers and the volumetric analysis of the tumor, which is / are relevant.

15. Have patients with advanced stage of cancer been treated with AIET?

YES. Patients with advances stage of cancer have been benefitted with AIET. For terminally ill patients we recommend an intensive course of four to six cycles of AIET within 45 days to start with. There are reports where breast cancer patients with multiple metastases have got a static disease for more than 15 months with 15 transfusions.

16. What are your results of AIET in terminally ill patients?

In general our Autologous Immune enhancement therapy has resulted in

a. Static non-progressive disease in 27% of the patients; which means 27% patients continued without further progression of the disease

b. Partial response in 23% of the patients; which means in 23 % of the patients, there was a significant reduction in size/volume of the tumour

c. Compete response in 2% of the patients; which means in these patients the tumour disappeared completely

d. Progression of the disease in rest of the patients

These are the results of a cumulative six month evaluation in patients with stage IV cancers of various organs