MEDLINE Abstracts

1. Activities and characteristics of transfer factors
2. Transfer factors: identification of conserved sequences in transfer factor molecules.
3. Immunomodulatory therapy of epilepsy with transfer factor
4. Immunotherapy with transfer factor of recurrent herpes simplex type I.
5. Lessons from a pilot study of transfer factor in chronic fatigue syndrome.
6. Transfer factor with anti-EBV activity as an adjuvant therapy for nasopharyngeal carcinoma: a pilot study.
7. Murine transfer factors: dose-response relationships and routes of administration.
8. Utility of transfer factor to detect different bronchodilator responses in patients with chronic obstructive pulmonary disease.
9. Comparative study of transfer factor and acyclovir in the treatment of herpes zoster.
10. Transfer factor in chronic mucocutaneous candidiasis.
11. Transfer factor as an adjuvant to non-small cell lung cancer (NSCLC) therapy.
12. The use of transfer factors in chronic fatigue syndrome: prospects and problems.
13. In vitro studies during long-term oral administration of specific transfer factor.
14. Orally administered HSV-specific transfer factor (TF) prevents genital or labial herpes relapses.
15. Use of transfer factor for the treatment of recurrent non-bacterial female cystitis (NBRC): a preliminary report.
16. Preliminary observations using HIV-specific transfer factor in AIDS.
17. Immunotherapy with transfer factor of recurrent herpes simplex type I.
18. A preliminary report on the use of transfer factor for treating stage D3 hormone-unresponsive metastatic prostate cancer.
19. The biological activity of the transfer factor induced by bacterial antigens
20. Human specific transfer factor to Staphylococcus aureus antigens
21. Use of **transfer factor** in allergic **bronchial asthma**
22. The usefulness of transfer factor in asthma associated with frequent infections.
23. **Transfer factor** and possible applications in gynecology.
24. Transfer factor in restoration of cell mediated immunity in lung cancer patients.

Activities and characteristics of transfer factors.

Biotherapy 1996;9(1-3):13-6 (ISSN: 0921-299X)
Kirkpatrick CH
Innovative Therapeutics, Inc. Denver, CO, USA.
This report summarizes three components of our transfer **factor** research program. Several **clinical studies** have used oral administration of transfer **factor** containing materials. Sceptics have rejected these findings by assuming that the acidic and enzymatic environment of the gastrointestinal tract would destroy the **factors**. To further examine this issue, we have conducted dose-response **studies** of the delayed-type hypersensitivity reaction in mice that were given transfer **factor** either by gavage or subcutaneously. There were no difference in the responses that were related to the route of administration. We conclude that oral route of administration is efficacious and should be used when possible. We have also **studied** the effects of transfer **factors** on immune responses by recipients. The details of this research are presented in the paper by Dr. Alvarez-Thull. Briefly, the **study** showed that recipients of a specific transfer **factor** responded to the antigen for which the **factor** was specific by secreting gamma-IFN, but no other cytokines. The structures of transfer **factor** molecules are unknown. We have developed a process for isolating transfer **factors** in pure form and we have obtained preliminary data concerning amino acid sequences. Our goal is to obtain the complete primary structure of several transfer **factor** molecules.

Transfer factors: identification of conserved sequences in transfer factor molecules.

Mol Med 2000 Apr;6(4):332-41 (ISSN: 1076-1551)
Kirkpatrick CH
Department of Medicine, University of Colorado Health Sciences Center, Denver, USA.
BACKGROUND: **Transfer factors** are small proteins that "**transfer**" the ability to express cell-mediated immunity from immune donors to non-immune recipients. We developed a process for purifying specific **transfer factors** to apparent homogeneity. This allowed us to separate individual **transfer factors** from mixtures containing several **transfer factors** and to demonstrate the antigen-specificity of **transfer factors**. **Transfer factors** have been shown to be an effective means for correction of deficient cellular immunity in patients with opportunistic infections, such as candidiasis or recurrent Herpes simplex and to provide prophylactic immunity against varicella-zoster in patients with acute leukemia. MATERIALS AND METHODS: **Transfer factors** of bovine and murine origin were purified by affinity chromatography and high performance liquid chromatography. Cyanogen bromide digests were sequenced. The properties of an apparently conserved sequence on expression of delayed-type hypersensitivity by **transfer factor** recipients were assessed. RESULTS: A novel amino acid sequence, LLYAQDL/VEDN, was identified in each of seven **transfer factor** preparations. These peptides would not **transfer** expression of delayed-type hypersensitivity to recipients, which indicates that they are not sufficient for expression of the specificity or immunological properties of native **transfer factors**. However, administration of the peptides to recipients of native **transfer factors** blocked expression of delayed-type hypersensitivity by the recipients. The peptides were not immunosuppressive. CONCLUSIONS: These findings suggest that the peptides may represent the portion of **transfer factors** that binds to the "target cells" for **transfer factors**. Identification of these cells will be helpful in defining the mechanisms of action of **transfer factors**.

Immunomodulatory therapy of epilepsy with transfer factor

Bratisl Lek Listy 1997 Apr;98(4):234-7 (ISSN: 0006-9248)
Simko M; Mokran V; Nyulassy S
Zdruzene lekarsko-imunologicke pracovisko Ustavu preventivnej a klinickej mediciny a Dererovej Nemocnice a poliklinikou v Bratislave, Slovakia.
Effect of immunotherapy with Transfer **factor** administered for a period of three months was **studied** in a group of ten epileptic patients, treated with carbamazepine or primidon previously and throughout the **study**. Out of eight patients, who finished the **study** we could notice significant reduction of epileptic discharges in eight patients. The results of this **study** prove that addition of immunomodulatory treatment to patients with intractable epilepsy could substantially improve the course of the disease in some patients. (Tab. 1, Fig. 5, Ref. 13.).

Immunotherapy with transfer factor of recurrent herpes simplex type I.

Arch Med Res 1995;26 Spec No:S87-92 (ISSN: 0188-4409)

Estrada-Parra S; Chavez-Sanchez R; Ondarza-Aguilera R; Correa-Meza B; Serrano-Miranda E; Monges-Nicolau A; Calva-Pellicer C
Departamento de Inmunologia, Escuela Nacional de Ciencias Biologicas, Instituto Politecnico Nacional, Mexico, D.F.

This **clinical** trial of Transfer **Factor**, an immunomodulator, in the treatment of herpes simplex type I, proved this agent to be more effective as regards duration of acute phase recurrences as well as the frequency of the reappearance of relapses of this disease. The evaluation was made in 20 patients whose disease had been treated before with other therapeutic agents (including acyclovir) which permitted them to be their own controls for the comparative data obtained and submitted to statistical analysis of the two parameters mentioned, duration of the acute phase and frequency of relapses. Patients with compromised cellular immunity or with any additional disease were excluded from the **study**. Transfer **factor**, one unit, was administered subcutaneously daily for 3 to 4 days during the acute phase of the disease, and subsequently at 15-day intervals for the first 6 months; followed by a continuation of monthly injections until the termination of the **study** period. In six of the 20 patients there was a recurrence of the disease while receiving maintenance dosages of TF. These patients were again given the full initial dosage schedule and reinstated again with the maintenance dosage. In the initial eight patients, an immune status profile was obtained, and all results were found to be in the normal range. This was considered sufficient evidence that the criteria for the selection of patients excluded any with detectable variations in the profile of the immune status, and it was decided to eliminate this as a prerequisite for participating in the **study**. The results showed an important improvement in the response to transfer **factor** immune modulation therapy. A statistically significant reduction in the frequency of recurrences within a one month period, the **Student** t test gave a p = 0.0001 in TF treated patients. The average duration in days of the acute phase also showed an important difference in favor of the TF treatment. The U Mann-Whitney test gave a p = 0.0005. These results suggest that, at present, TF may be considered the therapeutic agent of choice in the treatment of herpes simplex type 1 disease.

Lessons from a pilot study of transfer factor in chronic fatigue syndrome.

Biotherapy 1996;9(1-3):87-90 (ISSN: 0921-299X)

De Vinci C; Levine PH; Pizza G; Fudenberg HH; Orens P; Pearson G; Viza D
Immunodiagnosis and Immunotherapy Unit, 1st Division of Urology Sant'Orsola-Malpighi Hospital, Bologna, Italy.

Transfer **Factor** (TF) was used in a placebo controlled pilot **study** of 20 patients with chronic fatigue syndrome (CFS). Efficacy of the treatment was evaluated by **clinical** monitoring and testing for antibodies to Epstein-Barr virus (EBV) and human herpes virus-6 (HHV-6). Of the 20 patients in the placebo-controlled trial, improvement was observed in 12 patients, generally within 3-6 weeks of beginning treatment. Herpes virus serology seldom correlated with **clinical** response. This **study** provided experience with oral TF, useful in designing a larger placebo-controlled **clinical** trial.

Transfer factor with anti-EBV activity as an adjuvant therapy for nasopharyngeal carcinoma: a pilot study.

Biotherapy 1996;9(1-3):109-15 (ISSN: 0921-299X)

Prasad U; bin Jalaludin MA; Rajadurai P; Pizza G; De Vinci C; Viza D; Levine PH
University of Malaya, Kuala Lumpur, Malaysia.

Overall survival of nasopharyngeal carcinoma (NPC) at UICC stage IV still remains unsatisfactory even with combination chemotherapy (CT) and radio-therapy (RT). In view of the association of reactivation of Epstein-Barr virus (EBV) with the development and recurrence of NPC, immunotherapy in the form of transfer **factor** (TF) with specific activity against EBV (TF-B1) was suggested as an adjuvant to a combination of CT and RT in order to improve survival. In the present **study**, 6 UICC stage IV patients received TF-B1 and another 6 patients matched for disease stage were given TF prepared from peripheral blood leucocytes (TF-PBL). Results were compared with another 18 patients matched by age, sex, and stage of disease who received standard therapy without TF during the same period (C group). After a median follow up of 47.5 months, the survival for the TF-B1 group was found to be significantly

better (P = < 0.05) than the PBL and C group. While the 8 patients with distant metastasis (DM), not treated with TF-B1 (6 in the control and 2 in the PBL group), died due to progressive disease (average survival being 14.3 months), both patients with DM in the TF-B1 group had complete remission: one died of tuberculosis after surviving for 3.5 years and another is still alive, disease free, after 4.2 years. Although the series involved a small number of cases, the apparent effect of adjuvant immunotherapy in the form of TF with anti-EBV activity is of considerable interest.

Murine transfer factors**: dose-response relationships and routes of administration.**

Cell Immunol 1995 Sep;164(2):203-6 (ISSN: 0008-8749)
Kirkpatrick CH; Hamad AR; Morton LC
Innovative Therapeutics, Inc., Denver, Colorado 80216, USA.
Transfer **factors** are protein immunomodulators that transfer the ability to express cell-mediated immunity from immunized donors to nonimmune recipients. The effects are antigen-specific. The experiments described in this report are a comparison of the relationship of the route of administration of various transfer **factors** to the magnitude of the delayed hypersensitivity responses (footpad swelling) to the corresponding antigen in the recipients. Three doses of each of four affinity-purified transfer **factor** preparations were **studied**. There were no significant differences in the footpad responses by recipients of either oral or subcutaneous transfer **factor**. These results support proposals for oral administration of transfer **factors** in **clinical** trials.

Utility of transfer factor **to detect different bronchodilator responses in patients with chronic obstructive pulmonary disease.**

Respiration 1998;65(4):282-8 (ISSN: 0025-7931)
Izquierdo-Alonso JL; Sanchez-Hernandez I; Fernandez Frances J; Castelao Naval J; Carrillo Arias F; Gallardo Carrasco J
Pneumology Department, Hospital Universitario de Guadalajara, Spain.
Previous **studies** have described that there are different types of disease in patients with established chronic obstructive pulmonary disease (COPD) with different **clinical** course and functional responses. The aim of this **study** was to evaluate if the presence of low transfer **factor** (LTF) values can predict the effectiveness of bronchodilator therapy, and to assess whether this group has different risk **factors** that may be related with the responses. Eighty patients with COPD were evaluated on three occasions. Initial assessment included a standard respiratory questionnaire, blood analysis, skin prick test and baseline lung function, all performed on the first visit. Bronchodilator response was evaluated after low (0.2 mg) and high (1 mg) doses of salbutamol, and after 2 weeks of oral prednisone. In patients with normal TLCO/VA % (NTF), a higher proportion of subjects with previous history of atopy was the only statistically significant difference compared to those with LTF (odds ratio 4.33; 95% confidence interval 1.06-25.15). Although the mean response in forced expiratory volume in 1 s (FEV1) to treatment was analogous in both groups, when bronchodilation was expressed as percent of predicted, there was a clear trend to a lower response in patients with LTF (0.2 mg salbutamol: 6.99 +/- 5.64 vs. 8.94 +/- 6. 61, p = 0.15; 1 mg salbutamol: 10.18 +/- 6.37 vs. 13.45 +/- 7.90, p < 0.05; oral prednisone: 5.51 +/- 6.94 vs. 8.74 +/- 10.81, p = 0.06). The percentage of patients who had >12% improvement from that predicted in FEV1 was also lower in this group (42 vs. 72%; p < 0. 05). Moreover, TLCO/VA% was significantly lower in those subjects with a negative bronchodilator trial with salbutamol (68 +/- 25 vs. 81 +/- 26; p < 0.05) and prednisone (69 +/- 26 vs. 90 +/- 22; p < 0. 01). In patients with LTF and NTF, airway responsiveness was only significantly related with basal airflow limitation (LTF, r = 0.44; NTF, r = 0.38). All other interaction terms were not statistically significant. These results indicate that in patiens with similar serverity of COPD, the presence of LTF indicates a decreased probability of a positive bronchodilator response, probably reflecting different pathological lesions. We suggest that transfer **factor** should be taken into consideration when bronchial response is evaluated in large **clinical** trials.

Comparative study **of transfer** factor **and acyclovir in the treatment of herpes zoster.**

Int J Immunopharmacol 1998 Oct;20(10):521-35 (ISSN: 0192-0561)
Estrada-Parra S; Nagaya A; Serrano E; Rodriguez O; Santamaria V; Ondarza R; Chavez R; Correa B; Monges A; Cabezas R; Calva C; Estrada-Garcia I

Department of Immunology, National School of Biological Sciences, National Polytechnic Institute, Prol. Carpio Y Plan de Ayala, Mexico, D.F. i-estrad@bios.encb.ipn.mx.

Reactivation of varicella herpes virus (VHV), latent in individuals who have previously suffered varicella, gives rise to herpes zoster and in some cases leads to a sequela of post herpetic neuritis with severe pain which is refractory to analgesics. Many different antiviral agents have been tried without achieving satisfactory results. Of all the antiviral agents employed, acyclovir has been the most successful in reducing post herpetic pain. However acyclovir has not been as reliable as interferon alpha (IFN-alpha). We have previously looked into the use of transfer **factor** (TF) as a modulator of the immune system, specifically with respect to its effectiveness in the treatment of herpes zoster. In this work findings from a comparative **clinical** evaluation are presented. A double blind **clinical** trial of TF vs acyclovir was carried out in which 28 patients, presenting acute stage herpes zoster, were randomly assigned to either treatment group. Treatment was administered for seven days and the patients were subsequently submitted to daily **clinical** observation for an additional 14 days. An analogue visual scale was implemented in order to record pain and thereby served as the **clinical** parameter for scoring results. The group treated with TF was found to have a more favorable **clinical** course, P < or = 0.015. Laboratory tests to assess the immune profile of the patients were performed two days prior and 14 days after initial treatment. The results of these tests showed an increase in IFN-gamma levels, augmentation in the CD4+ cell population but not the percentage of T rosettes in the TF treated group. These parameters were however insignificantly modified in patients receiving acyclovir. Although TF treated patients showed an increase in CD4+ counts these cells remained below the levels for healthy individuals. The **fact** that IFN-gamma levels as well as the counts for CD4+ cells rose in the TF treated group and not in the acyclovir one is very significant and confirms the immunomodulating properties of TF.

Transfer factor **in chronic mucocutaneous candidiasis.**

Biotherapy 1996;9(1-3):97-103 (ISSN: 0921-299X)

Masi M; De Vinci C; Baricordi OR
Department of Pediatrics, University of Bologna, Italy.

Fifteen patients suffering from chronic mucocutaneous candidiasis were treated with an in vitro produced TF specific for Candida albicans antigens and/or with TF extracted from pooled buffy coats of blood donors. CMI of the patients was assessed using the LMT and the LST in presence of candidine. The aim of the **study** was the **clinical** evaluation of TF treatment and the incidence of positive tests before, during, and after therapy. Immunological data were matched using the Chi square test. 87 LMT were performed for each antigen dose and at the dilution of 1/50, 58.9% (33/56) tests were positive during non-treatment or non-specific TF treatment. On the contrary 83.9% (26/31) were positive during specific TF treatment (P < 0.05). In the LST, a significant decrease of thymidine uptake in the control cultures in presence of autologous or AB serum was observed when patients were matched according to non-treatment, and both non specific (P < 0.05) and specific TF treatment (P < 0.01). Only during specific TF treatment was a significant increase of reactivity against the Candida antigen at the highest concentration noticed, when compared with the period of non specific treatment (P < 0.01). **Clinical** observations were encouraging: all but one patient experienced significant improvement during treatment with specific TF. These data confirm that orally administered specific TF, extracted from induced lymphoblastoid cell-lines, increases the incidence of reactivity against Candida antigens in the LMT. LST reactivity appeared not significantly increased with respect to the periods of non treatment, but was significantly increased when it was compared to the non-specific TF treatment periods. At the same time, a **clinical** improvement was noticed.

Transfer factor **as an adjuvant to non-small cell lung cancer (NSCLC) therapy.**

Biotherapy 1996;9(1-3):117-21 (ISSN: 0921-299X)

Pilotti V; Mastrorilli M; Pizza G; De Vinci C; Busutti L; Palareti A; Gozzetti G; Cavallari A
Istituto di Clinica Chirurgica II, S. Orsola-Malpighi, Bologna, Italy.

The rationale for using transfer **factor** (TF) in lung cancer patients is that the possibility of improving their cell-mediated immunity to tumour associated antigens (TAA) may improve their survival. From Jan 1984 to Jan 1995, 99 non-small cell lung cancer (NSCLC) resected patients were monthly treated with TF, extracted from the lymphocytes of blood bank donors. In the same period, 257 NSCLC resected patients were considered as non-treated controls. The survival rates of the TF treated group appear significantly improved both for patients in stages 3a and 3b, and patients with histological subtype "large cell carcinoma" (P < 0.02). Survival of TF treated patients is also significantly higher (P < 0.02) for patients with lymph node involvement (N2 disease). The results of this **study** suggest that the administration of TF to NSCLC resected patients may improve survival.

The use of transfer factors in chronic fatigue syndrome: prospects and problems.

Biotherapy 1996;9(1-3):77-9 (ISSN: 0921-299X)
Levine PH
Viral Epidemiology Branch, National Cancer Institute, Bethesda, MD, USA.
Chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by severe prolonged unexplained fatigue and a variety of associated symptoms such as arthralgias, myalgias, cognitive dysfunction, and severe sleep disturbances. Many patients initially present with an acute onset of apparent infectious origin with either an upper respiratory or gastrointestinal illness, fever, chills, tender lymphadenopathy, and malaise suggestive of a flu-like illness. In some cases, specific viral infections can be identified at the outset, particularly herpes viruses such as Epstein-Barr virus (EBV), human herpes virus-6 (HHV-6), and cytomegalovirus (CMV). Transfer **factors** (TF) with specific activity against these herpes viruses has been documented. With some **studies** suggesting that persistent viral activity may play a role in perpetuation of CFS symptoms, there appears to be a rationale for the use of TF in patients with CFS and recent reports have suggested that transfer **factor** may play a beneficial role in this disorder. This report focuses on the heterogeneity of CFS, the necessity for randomized coded **studies**, the importance of patient selection and sub-classification in **clinical** trials, and the need to utilize specific end-points for determining efficacy of treatment.

In vitro studies during long-term oral administration of specific transfer factor.

Biotherapy 1996;9(1-3):175-85 (ISSN: 0921-299X)
Pizza G; De Vinci C; Fornarola V; Palareti A; Baricordi O; Viza D
Immunodiagnosis and Immunotherapy Unit, S. Orsola Malpighi Hospital, Bologna, Italy.
153 patients suffering from recurrent pathologies, i.e. viral infections (keratitis, keratouveitis, genital and labial herpes) uveitis, cystitis, and candidiasis were treated with in vitro produced transfer **factor** (TF) specific for HSV-1/2, CMV and Candida albicans. The cell-mediated immunity of seropositive patients to HSV-1/2 and/or CMV viruses was assessed using the leucocyte migration inhibition test (LMT) and lymphocyte stimulation test (LST) in presence of the corresponding antigens, and the frequency of positive tests before, during and after TF administration was **studied**. The data were stratified per type of test, antigen and the recipients' pathology, and statistically evaluated. For the LMT, a total of 960 tests were carried out for each antigen dilution, 3 different antigen dilutions were used per test. 240/960 tests (25.4%) were found positive during non-treatment or treatment with unspecific TF, whereas 147/346 tests (42.5%) were found positive when the antigen corresponding to the specificity of the TF administered to the patient was used ($P < 0.001$). When the data were stratified following pathology, a significant increased incidence of positive tests during specific treatment was also observed ($0.0001 < P < 0.05$). In the LST (1174 tests), a significant increase of thymidine uptake was observed in the absence of antigen (control cultures), during treatment with both specific and unspecific TF, but also in the presence of antigen and/or autologous serum during specific TF administration ($P < 0.0001$). TF administration also significantly increased the soluble HLA class I antigens level in 40 patients **studied** to this effect.

Orally administered HSV-specific transfer factor (TF) prevents genital or labial herpes relapses.

Biotherapy 1996;9(1-3):67-72 (ISSN: 0921-299X)
Pizza G; Viza D; De Vinci C; Palareti A; Cuzzocrea D; Fornarola V; Baricordi R
Immunodiagnosis and Immunotherapy Unit, 1st-Division of Urology, S. Orsola-Malpighi Hospital, Bologna, Italy.
Forty-four patients suffering from genital (22) and labial (22) herpes were orally treated with HSV-1/2-specific transfer **factor** (TF). TF was obtained by in vitro replication of a HSV-1/2-specific bovine dialysable lymphocyte **extract**. Treatment was administered bi-weekly the first 2 weeks, and then weekly for 6 months, most patients received 2-3 courses. The total observation period for all patients before treatment was 26,660 days, with 544 relapses, and a relapse index of 61.2, whereas the cumulative observation period during and after treatment was 16,945 days, with a total of 121 relapsing episodes and a cumulative RI of 21.4 ($P < 0.0001$). Results were equally significant when the 2 groups

of patients (labial and genital) were considered separately. These observations confirm previous results obtained with bovine HSV-specific TF, and warrant further studies to establish HSV-specific TF as a choice of treatment for preventing herpes recurrences.

Use of transfer factor for the treatment of recurrent non-bacterial female cystitis (NBRC): a preliminary report.

Biotherapy 1996;9(1-3):133-8 (ISSN: 0921-299X)

De Vinci C; Pizza G; Cuzzocrea D; Menniti D; Aiello E; Maver P; Corrado G; Romagnoli P; Dragoni E; Lo Conte G; Riolo U; Masi M; Severini G; Fornarola V; Viza D
Immunodiagnosis and Immunotherapy Unit, 1st-Division of Urology, Bologna, Italy.

Results of conventional treatment of female non-bacterial recurrent cystitis (NBRC) are discouraging. Most patients show an unexpected high incidence of vaginal candidiasis, while their cell mediated immunity to Herpes simplex viruses (HSV) and Candida antigens seems impaired, and it is known that the persistence of mucocutaneous chronic candidiasis is mainly due to a selective defect of CMI to Candida antigens. Twenty nine women suffering of NBRC, and in whom previous treatment with antibiotics and non-steroid anti-inflammatory drugs was unsuccessful, underwent **oral** transfer **factor** (TF) therapy. TF specific to Candida and/or to HSV was administered bi-weekly for the first 2 weeks, and then once a week for the following 6 months. No side effects were observed during treatment. The total observation period of our cohort was 24379 days with 353 episodes of cystitis recorded and a cumulative relapse index (RI) of 43. The observation period during and after treatment was 13920 days with 108 relapses and a cumulative RI of 23 ($P < 0.0001$). It, thus, seems that specific TF may be capable of controlling NBRC and alleviate the symptoms.

Preliminary observations using HIV-specific transfer factor in AIDS.

Biotherapy 1996;9(1-3):41-7 (ISSN: 0921-299X)

Pizza G; Chiodo F; Colangeli V; Gritti F; Raise E; Fudenberg HH; De Vinci C; Viza D
Immunodiagnosis and Immunotherapy Unit, Ospedale S. Orsola-Malpighi, Bologna, Italy.

Twenty five HIV-1-infected patients, at various stages (CDC II, III and IV) were treated orally with HIV-1-specific transfer **factor** (TF) for periods varying from 60 to 1870 days. All patients were receiving antiviral treatments in association with TF. The number of lymphocytes, CD4 and CD8 subsets were followed and showed no statistically significant variations. In 11/25 patients the number of lymphocytes increased, whilst in 11/25 decreased; similarly an increase of the CD4 lymphocytes was observed in 11/25 patients and of the CD8 lymphocytes in 15/25. Clinical improvement or a stabilized clinical condition was noticed in 20/25 patients, whilst a deterioration was seen in 5/25. In 12/14 anergic patients, daily TF administration restored delayed type hypersensitivity to recall antigens within 60 days. These preliminary observations suggest that **oral** HIV-specific TF administration, in association with antiviral drugs, is well tolerated and seems beneficial to AIDS patients, thus warranting further investigation.

Immunotherapy with transfer factor of recurrent herpes simplex type I.

Arch Med Res 1995;26 Spec No:S87-92 (ISSN: 0188-4409)

Estrada-Parra S; Chavez-Sanchez R; Ondarza-Aguilera R; Correa-Meza B; Serrano-Miranda E; Monges-Nicolau A; Calva-Pellicer C
Departamento de Inmunologia, Escuela Nacional de Ciencias Biologicas, Instituto Politecnico Nacional, Mexico, D.F.

This clinical trial of **Transfer Factor**, an immunomodulator, in the treatment of herpes simplex type I, proved this agent to be more effective as regards duration of acute phase recurrences as well as the frequency of the reappearance of relapses of this **disease**. The evaluation was made in 20 patients whose **disease** had been treated before with other therapeutic agents (including acyclovir) which permitted them to be their own controls for the comparative data obtained and submitted to statistical analysis of the two parameters mentioned, duration of the acute phase and frequency of relapses. Patients with compromised cellular immunity or with any additional **disease** were excluded from the study. **Transfer factor**, one unit, was administered subcutaneously daily for 3 to 4 days during the acute phase of the **disease**, and subsequently at 15-day intervals for the first 6 months; followed by a continuation of monthly injections until the termination of the study period. In six of the 20 patients there was a recurrence of the **disease** while receiving maintenance dosages of TF. These patients were again

given the full initial dosage schedule and reinstated again with the maintenance dosage. In the initial eight patients, an immune status profile was obtained, and all results were found to be in the normal range. This was considered sufficient evidence that the criteria for the selection of patients excluded any with detectable variations in the profile of the immune status, and it was decided to eliminate this as a prerequisite for participating in the study. The results showed an important improvement in the response to **transfer factor** immune modulation therapy. A statistically significant reduction in the frequency of recurrences within a one month period, the Student t test gave a p = 0.0001 in TF treated patients. The average duration in days of the acute phase also showed an important difference in favor of the TF treatment. The U Mann-Whitney test gave a p = 0.0005. These results suggest that, at present, TF may be considered the therapeutic agent of choice in the treatment of herpes simplex type 1 **disease**.

A preliminary report on the use of transfer factor **for treating stage D3** hormone**-unresponsive metastatic prostate** cancer**.**

Biotherapy 1996;9(1-3):123-32 (ISSN: 0921-299X)

Pizza G; De Vinci C; Cuzzocrea D; Menniti D; Aiello E; Maver P; Corrado G; Romagnoli P; Dragoni E; Lo Conte G; Riolo U; Palareti A; Zucchelli P; Fornarola V; Viza D
Immunodiagnosis and Immunotherapy Unit, S. Orsola-Malpighi Hospital, Bologna, Italy.

As conventional treatments are unsuccessful, the survival rate **of** stage D3 prostate **cancer** patients is poor. Reports have suggested the existence **of** humoral **and cell**-mediated immunity (CMI) against prostate **cancer** tumour-**associated** antigens (TAA). These observations prompted us to treat stage D3 prostate **cancer** patients with an **in** vitro produced **transfer factor** (TF) able to **transfer**, **in** vitro **and in** vivo, CMI against **bladder and** prostate TAA. Fifty patients entered this **study and** received one intramuscular injection **of 2**-5 units **of** specific TF monthly. Follow-up, ranging from **1** to 9 years, showed that complete remission was achieved **in 2** patients, partial remission **in** 6, **and** no progression **of** metastatic **disease in** 14. The median survival was 126 weeks, higher than the survival rates reported **in** the literature for patients **of** the same stage.

The biological activity of the transfer factor **induced by bacterial antigens**

[Biolohichna aktyvnist' faktora perenosu, indukovanoho bakterial'nymy antyhenamy.]

Mikrobiol Z 1997 Sep-Oct;59(5):83-100

Liubchenko TA; Holeva OH; Kholodna LS; Smirnov VV; Vershyhora AIu

Today's statement of **transfer factor**, an immunostimulator derived from leukocytes which enhances antiinfectious immunity, is observed in the review. Basic biological, physical and chemical characteristics of the **transfer factor**, its possible action mechanisms, and laboratory and clinical methods of use to cure infectious fungal (Candida, Coccidium), invasive (schistosomiasis, leishmaniasis, cryptosporidiosis), viral (varicella zoster, ophthalmic herpes, Herpes simplex types 1 and 2, H. zoster, H. simplex ceratitis, genital herpes, human herpes virus type 6, postherpetic neuritis, hepatitis B, AIDS), and bacterial infections (Mycobacterium leprae, M. tuberculosis, M. fortuitum, Salmonella cholerae suis, S. dublin, S. Virchov, Brucella abortus, Actinobacillus pleuropneumoniae, bacterial sepsis, Staphylococcus) are described.

Human specific transfer factor **to Staphylococcus aureus antigens**

[Liuds'kyij spetsyfichnyij Faktor perenosu do antyheniv Staphylococcus aureus.]

Fiziol Zh 1997;43(3-4):25-32

Liubchenko TA; Holeva OH; Kholodna LS; Stepanchuk VA; Vershyhora AIu

Immunobiological properties of human specific **transfer factor** (TF) to Staphylococcus aureus antigens were studied. It is shown that this TF activated human leucocytes in vitro as well as in vivo. Antigen specificity of TF's immunomodulating effects is also shown. In vitro we used leucocyte migration inhibition test (IML), macrophage inhibition test (MPI) and rosette formation (E-ros). For testing in vivo we used delayed type hypersensitivity (DTH) skin tests.

Use of transfer factor in allergic bronchial asthma

[Uso del **factor** de transferencia en el asma bronquial alergica.]

Rev Alerg 1993 Mar-Apr;40(2):42-5
Salazar Villa RM; Mejia Ortega J
Servicio de alergia e inmunologia clinica, Hospital de Especialidades, Centro Medico Nacional Siglo XXI.
The therapeutic panorama of immunomodulation and its effects on the modification of the immune reaction is reviewed. Particular reference is made to the **transfer factor** as a therapeutic element in **bronchial asthma**, which insures its efficacy or innocuity.

The usefulness of transfer factor **in** asthma **associated with frequent infections.**

Ann Allergy 1978 Apr;40(4):229-32 (ISSN: 0003-4738)
Khan A; Sellars W; Grater W; Graham MF; Pflanzer J; Antonetti A; Bailey J; Hill NO
Fifteen patients underwent controlled trial with **transfer factor** for repeated infections and severe **asthma**. Marked decrease in respiratory infections and striking improvement in **asthma** resulted. The authors suggest that **transfer factor** may reconstitute immune function, thus representing a unique approach to severe **asthma** associated with frequent infections.

Transfer factor **and possible applications in gynecology.**

Am J Obstet Gynecol 1978 Mar 1;130(5):572-84 (ISSN: 0002-9378)
Freedman RS; Wharton JT; Rutledge F; Sinkovics JG
Dialyzable transfer factor (TFd) is reviewed against its historical background, preparation methods, physiochemical properties, possible mechanisms of action, pharmacology, and clinical **studies**, including several areas relating to gynecology. The possible role of TFd as an adjunct in the treatment of cancer is discussed. The discussion centers on gynecologic cancer in several patients who have received TFd. The difficulties and future possibilities for this modality of treatment are considered.

Transfer factor **in restoration of cell mediated immunity in** lung **cancer patients.**

Jpn J Surg 1983 Jul;13(4):304-11 (ISSN: 0047-1909)
Fujisawa T; Yamaguchi Y; Kimura H
We **studied** the **transfer factor** (TF) with regard to in vivo and in vitro restoration of cell mediated immunity (CMI) in **lung** cancer patients. Twenty-eight **lung** cancer patients who had undergone resection were the recipients and 30 household **contact** family members with a positive reactivity to **lung** cancer **extract** were the donors of TF. Immunologic **status** was evaluated by **delayed** type **cutaneous hypersensitivity** (DTH), peripheral T lymphocyte number, PHA lymphocyte blastogenesis, **serum** blocking activity (SBA) and leucocyte adherence inhibition (LAI) test. When TF was administered twice subcutaneously to the patients, there was a statistically significant restoration or augmentation of DTH, PHA lymphocyte blastogenesis and abrogation of SBA, particularly in patients with suppressed CMI. These results suggest that it was the TF obtained from relatives of **lung** cancer patients with positive reactivity to tumor associated antigens restored or augmented tumor specific and nonspecific CMI in these **lung** cancer patients.