Birth Defects Orig Artic Ser. 1975;11(1):441-4. Related Articles, Links

Restoration of cell-mediated immune responses with transfer factor.

Kirkpatrick CH.

Five anergic patients with chronic mucocutaneous candidiasis were given transfer factor from donors with positive delayed reactions to Candida. In each recipient, the delayed skin reactions of the transfer factor donors appeared in the recipients and no recipient developed reactivities not possessed by the donor. Prior to injection of transfer factor, in vitro stimulation of the patients' lymphocytes with antigens did not result in MIF production, however, after transfer factor this response was positive. Therapy with transfer factor alone did not have therapeutic benefit, however, in 2 patients treatment with amphotericin-B followed by transfer factor has produced cutaneous remissions of 18 months.

PMID: 1096989 [PubMed - indexed for MEDLINE]
Birth Defects Orig Artic Ser. 1975;11(1):431-5. Related Articles, Links

Use of transfer factor in patients with depressed cellular immunity and chronic infection.

Rocklin RE.

Two patients with chronic mucocutaneous candidiasis and a defect in cellular immunity received a single injection of dialysable transfer factor from Candida-positive donors in an effort to reconstitute immunologic function. The transfer of cellular hypersensitivity was successful in one of the two patients and was monitored by skin tests and MIF production; however, the effect was temporary and did not change the clinical course of the patient's infection. The other patient did not respond eitherimmunologically or clinically to transfer factor at this time, although she did respond subsequently to repeated doses of transfer factor and amphotericin B therapy (Pabst and Swanson: Brit. med. J. 2:442, 1972). In another instance transfer factor from tuberculin-positive donors was used successfully to eradicate an infection in a patient with progressive primary tuberculosis and an acquired defect in cellular immunity. The patient had not responded clinically or bacteriologically after 7 1/2 months of antituberculous therapy, although the organism was shown to be sensitive in vitro to the drugs she was receiving. She received 6 doses of dialysable transfer factor over a 3-month period and during this time she responded clinically, bacteriologically and roentgenographically.

PMID: 1096987 [PubMed - indexed for MEDLINE]
1: Birth Defects Orig Artic Ser. 1975;11(1):436-40.
Related Articles, Links

Transfer factor as an approach to the treatment of immune deficiency disease.

Schulkind ML, Ayoub EM.

Use of transfer factor in the treatment of chronic mucocutaneous candidiasis is discussed. The clinical experience in treating 2 patients with different clinical expressions of the syndrome and their different responses to treatment with repeated injections of transfer factor given in conjunction with amphotericin-B are reported. Results indicate that this form of therapy is a safe and effective way of restoring cell-mediated immunity to Candida and successfully treating some patients with chronic mucocutaneous candidiasis.

PMID: 1096988 [PubMed - indexed for MEDLINE]
Arch Dermatol. 1979 Feb;115(2):180-4. Related Articles, Links

Immunologic features of chronic granulomatous mucocutaneous candidiasis before and after treatment with transfer factor.

Horsmanheimo M, Krohn K, Virolainen M, Blomqvist K.

We report the acquisition of skin test sensitivity to Candida albicans antigen and the ability to produce leukocyte migration inhibition factor (MIF) by a Candida-negative patient with chronic granulomatous mucocutaneous candidiasis after treatment with dialyzable transfer factor (TFd). The TFd was acquired from Candida-positive healthy donors. Three of seven attempts to transfer Candida skin test sensitivity were successful, and the acquired skin reactivity lasted for 12 to 21 days. The acquisition of cellular immunity to Candida was demonstrated in vitro by production of leukocyte MIF. No Candida-induced lymphocyte transformation was observed before or after TFd injection. The TFd did not cause Candida-induced blast transformation when added directly to cultures of lymphocytes from the patient. Pain, tenderness, redness,

and edema were observed around the Candida granulomas on each occasion when the skin test to Candida became positive. Two weeks after TDd injection, the proliferative response of peripheral blood lymphocytes increased, as measured by incorporation of tritiated thymidine into lymphocytes within the first hour of in vitro incubation.

Publication Types:
• Case Reports

PMID: 426525 [PubMed - indexed for MEDLINE]
Invest Dermatol. 1977 Jan;68(1):10-5. Related Articles, Links

Clinical study of a patient with lupus vulgaris before and after injection of dialyzable transfer factor.

Horsmanheimo M, Krohn K, Virolainen M.

This report describes the clinical improvement and acquisition of tuberculin skin-test sensitivity by a tuberculin-negative, drug-resistant patient with lupus vulgaris after a single injection of dialyzable transfer factor (TFd) from a tuberculin-positive healthy donor. The patient's lymphocytes showed a slight response to tuberculin in the leukocyte migration inhibition test and in the lymphocyte transformation test before TFd injection. The acquisition of cellular immunity to tuberculin was demonstrated in vitro by enhanced tuberculin-induced blast transformation. A good correlation between skin test and in vitro tuberculin sensitivity and clinical improvement was seen during the three years that the patient was observed.

Publication Types:
• Case Reports

PMID: 318672 [PubMed - indexed for MEDLINE]
Intern Med. 1981 Mar;141(4):533-7. Related Articles, Links

Transfer factor therapy for histoplasmosis in a patient with Hodgkin's disease.

Catanzaro A, Spitler LE, Campbell GD, Moser KM.

A patient with recurrent chronic histoplasmosis was diagnosed also as having Hodgkin's disease. Studies of cell-mediated immunity (CMI) demonstrated no reaction to histoplasmin by skin test, lymphocyte transformation (LT), or leukocyte inhibition factor (LIF) assay. Clinical and immunologic studies were performed during treatment with 19 doses of dialyzable transfer factor (TF) prepared from a normal donor with strong CMI against histoplasmin. Transfer of CMI to the patient was demonstrated by all three tests. All tests reverted to nonreactive during the period of observation. Repeated doses of dialyzable TF were followed by reconversion of skin tests. The LIF assay was most reactive. Reactivation of histoplasmosis occurred during antimetabolic therapy for Hodgkin's disease; however, the lesions cleared rapidly when TF was added to amphotericin B. Amphotericin B was administered at a dosage of 25 mg three times each week during the entire study.

Publication Types:
• Case Reports

PMID: 7212899 [PubMed - indexed for MEDLINE]
Eur J Cancer Clin Oncol. 1988 May;24(5):929-33. Related Articles, Links

Transfer factor in Hodgkin's disease: a randomized clinical and immunological study.

Hancock BW, Bruce L, Sokol RJ, Clark A.

University Department of Medicine, Royal Hallamshire Hospital, Sheffield, U.K.

Transfer factor (TF) was prepared from buffy coats obtained from 493 units of blood taken from healthy donors, including individuals convalescent from various viral infections. It was administered to 22 of 47 patients with Hodgkin's disease undergoing treatment and consenting to take part in this randomized study to determine if TF would enhance their immunity and/or reduce the incidence of subsequent infections. Skin test reactivity was markedly enhanced in those patients receiving TF as opposed to placebo but other immunological assessments showed no significant differences between the groups. TF was not shown to be of benefit in the prevention of infections (including varicella/zoster).

Publication Types:

• Clinical Trial
• Randomized Controlled Trial

PMID: 3049116 [PubMed - indexed for MEDLINE]
Boll Ist Sieroter Milan. 1976;55(2):168-73. Related Articles, Links

Aspecific transfer factor in children with Hodgkin's disease.

Pasino M, Vadala CR, Tonini GP, Comelli A, Perutelli P.

Six children suffering from Hodgkin's disease (HD), in different stages and free from chemo- and radiotherapy from at least four weeks, were treated with transfer factor (TF). PPD skin test, PHA-responsiveness, E-rosettes, B-lymphocytes were checked before TF therapy, after 6 and 9 TF doses and compared to the data at the onset of the disease. Two children with HD who did not receive TF, were examined as controls. PPD skin tests, PHA-responsiveness, E-rosettes did not ameliorate following TF treatment, while it has been noticed an increase in B-lymphocytes, both in percentage and absolute number. The Authors conclude that TF might have induced a slight B lymphoproliferation.

PMID: 1088071 [PubMed - indexed for MEDLINE]
Ann Allergy. 1976 May;36(5):330-6. Related Articles, Links

Increase in E-rosettes after transfer factor (TF) treatment: fractionation of TF.

Khan A, Thometz D, Garrison O, Hill JM.

The effect of transfer factor (TF) on E-rosettes (ER) was studied in vivo in a patient with Hodgkin's disease. Transfer factor was given in doses of 10 units/sq m intramuscularly. The ER forming cells and the ER scores were determined. The ER score method took into account the number of erythrocytes in each rosette. The increase in ER score was maximum at 24 hours and it declined during the following one to two weeks. It was suggested that TF may have to be given more frequently than indicated by the persistence of skin reactivity. TF was fractionated with high pressure liquid chromatography. Fraction 2 increased ER in a patient with Schwannoma. Non-specificity of TF was also discussed.

Publication Types:
• Case Reports

PMID: 1084716 [PubMed - indexed for MEDLINE]
Cancer. 1975 Jul;36(1):86-9. Related Articles, Links

Improvement in delayed hypersensitivity in Hodgkin's disease with transfer factor: lymphapheresis and cellular immune reactions or normal donors.

Khan A, Hill JM, MacLellan A, Loeb E, Hill NO, Thaxton S.

Passive transfer of delayed hypersensitivity was achieved, with normal transfer factor, in patients with Hodgkin's disease in remission. The cellular immune responses of the recipients improved. It is suggested that, in addition to specific effect the transfer factor (or factors) has a nonspecific effect causing improvement in the state of delayed hypersensitivity of the recipient in general. The average number of E-rosette T lymphocytes was 46.3% after the transfer factor treatment in Hodgkin's disease. The control patients with Hodgkin's disease, not receiving transfer factor, had a value of 37.8%. Removal of 4.9 X 10(9) to 1.08 X 10(10) lymphocytes did not diminish the delayed hypersensitivity of the donor. Side effects attributable to transfer factor were not seen.

PMID: 1081903 [PubMed - indexed for MEDLINE]
Lancet. 1975 Nov 8;2(7941):901-3. Related Articles, Links

Transfer factor in Hodgkin's disease.

Ng RP, Moran CJ, Alexopoulos CG, Bellingham AJ.

In a controlled studiy, six patients with stage-IV Hodgkin's disease were given transfer factor (T.F.) prepared from patients with Hodgkin's disease in long remission. There was an apparent increase in cell-mediated immune responses as evidenced by a significant increase in the recipients' lymphocyte responses to phytohaemagglutinin stimulation. Three out of six patients converted to positive delayed-hypersensitivity tests. These three all had the nodular sclerosing type of

Hodgkin's disease. These results warrant the further investigation of the use of Hodgkin's disease-specific T.F. as a therapeutic agent in this condition.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 53376 [PubMed - indexed for MEDLINE]
Acta Paediatr Scand. 1977 Mar;66(2):211-7. Related Articles, Links

Transfer factor in chronic and recurrent respiratory tract infections in children.

Grohn P.

Five cases with abnormal sensitivity to respiratory tract infections are described. The cases showed a marked impairment in their cell mediated immunity state. Administration of a chromatographically purified transfer factor component increased the skin test sensitivity to common recall antigens. Interestingly, a similar effect in skin reactivity was observed with repeated skin tests alone, when antigen concentrations, initially high enough to cause a positive reaction, were used. Neither the administration of transfer factor nor skin testing with high antigen concentrations had an effect on blast transformation percentages. The therapy with chromatographically purified transfer factor appeared promising on the clinical condition of the patients.

Publication Types:
• Case Reports
• Clinical Trial

PMID: 320816 [PubMed - indexed for MEDLINE]
Acta Paediatr Scand. 1977 Mar;66(2):219-24. Related Articles, Links

Transfer factor and cellular immune response in urinary tract infections in children.

Anttila R, Grohn P, Krohn K.

Cellular immune responses in vivo and in vitro were studied in 20 children with chronic or relapsing urinary tract infections. Skin tests revealed decreased immune responses to PPD in cases with chronic or recurrent pyelonephritis and to OM, in these cases and in cases of lower urinary tract infections. Blast transformation responses to PPD, OM and PHA were at least as high as in controls. Administration of chromatographically purified fraction from human leucocyte transfer factor resulted in a positive skin reaction with antigen concentration, which before TF administration had caused a negative reaction. The results suggest that the action of the transfer factor component used in this study is based on an immunologically nonspecific stimulation of the cellular immune response.

Publication Types:
• Clinical Trial

PMID: 320817 [PubMed - indexed for MEDLINE]
1: Scand J Rheumatol. 1976;5(3):151-7. Related Articles, Links

The effect of non-specifically acting transfer factor component on cellular immunity in juvenile rheumatoid arthritis.

Grohn P, Anttila R, Krohn K.

A chromatographically purified component of human dialysable transfer factor with a non-specific stimulatory effect on the expression of immune response was used in a therapeutic trial in 8 cases of juvenile rheumatoid arthritis. Enhancement of the delayed type of immune response, measured by skin testing, was seen in all cases, but in vitro reactions to test antigens were unaltered. Clinical improvement was seen in all patients with acute history and in 2 of the 5 chronic cases, but it is not certain whether this was caused by the improved immune reactivity, or whether this reflected the known variable natural history of the disease.

PMID: 981991 [PubMed - indexed for MEDLINE]
Ann Rheum Dis. 1978 Apr;37(2):175-9. Related Articles, Links

No effect of transfer factor in juvenile rheumatoid arthritis by double-blind trial.

Hoyeraal HM, Froland SS, Salvesen CF, Munthe E, Natvig JB, Kass E, Blichfeldt P, Hegna TM, Revlem E, Sandstad B, Hjort NL.

A previously pilot study of treatment with transfer factor in 3 patients with juvenile rheumatoid arthritis (JRA) gave promising results. However, in this small and open study no definite conclusions could be drawn. Therefore, a double-blind group trial was performed in 12 JRA patients treated with transfer factor, and in 12 placebo-treated control patients. The patients were evaluated clinically, by laboratory tests, and by estimation of different lymphocyte populations and cell-mediated immunity in vitro and in vivo. Transfer factor was not found to be of significant therapeutic value in patients with JRA. The only statistically significant difference between the two groups was a greater reduction in the percentage of T lymphocytes in transfer factor-treated patients than in control patients. The significance of this is difficult to explain and could have appeared by chance. No side effects of treatment with transfer factor were noted.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 348131 [PubMed - indexed for MEDLINE]
1: Immunology. 1979 Jan;36(1):1-12. Related Articles, Links

Cellular immunity in patients with the Wiskott-Aldrich syndrome before and after administration of transfer factor: a follow-up study.

Schut BJ, Dooren LJ, Uittenbogaart CH, Schellekens PT, Eijsvoogel VP.

Four patients with Wiskott-Aldrich syndrome were treated with transfer factor (TF), in an attempt to improve their clinical condition. Before and during treatment, cellular reactivity was followed in vivo (delayed type skin reactivity) and in vitro (lymphocyte transformation). In all patients positive skin reactions were occasionally observed during TF treatment. The lymphocyte reactivity in vitro to phytohaemagglutinin (PHA) was slightly diminished, the responding capacity of the mixed lymphocyte culture (MLC) severely impaired and the response to bacterial, viral and fungal antigens absent before and during TF treatment. No clinical improvement was observed after large doses of TF. No correlation between skin test reversal and TF administration was found, and lymphocyte transformation in vitro did not improve. Subsequently, a double blind trial, in which we compared the effect of TF and placebo, was carried out in these patients, which revealed no effect of TF therapy. It is concluded that the results of treatment with TF in these patients are highly controversial.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial
Лепра

Cell mediated immunity in patients with Virchowian hanseniasis before and after treatment with transfer factor.

Leser PG, Margarido L, Belda W, Sartori SG, Hares WA, Freire CA, Fleury R, Montenegro MR, Leser W, Naspitz CK.

PMID: 369991 [PubMed - indexed for MEDLINE]
Cell mediated immunity (CMI), bacterial index (BI), morphological index (MI), skin and lymph nodes biopsies were evaluated in 15 patients with virchowian hanseniasis before and after treatment with transfer factor (TF) obtained from human spleens. The patients were divided in 3 groups: group I (control) received only sulfone, group II received sulfone plus TF and group III received only TF. There was no difference in the numbers of peripherical T and B lymphocytes of patients and normal controls. Before the treatment with TF, there was an impaired response of the patient's peripheral lymphocytes to PHA stimulus, in the presence of autologous or homologous plasma. This depressed response was corrected after treatment with TF in the patients of group III. In none of the patients a positive Mitsuda reaction was observed before and after treatment with TF. The improvement of the MI observed in group III, treated only with TF was remarkably similar to the patients treated only with sulfone. This work points out that TF has a role in the treatment of patients with virchowian hanseniasis, based on the improvement of CMI, MI, on histopathology of skin biopsies and clinical conditions.

Am J Trop Med Hyg. 1978 Sep;27(5):995-1004. Related Articles, Links

Reversal reactions in lepromatous leprosy following transfer factor therapy.

Hastings RC, Job CK.

Five patients with active leprosy, four with polar lepromatous (LL) and one with borderline lepromatous (BL) disease, were each treated with transfer factor (TF) from approximately 7.4 x 10(9) lymphocytes given in 36 divided doses over a 12-week period. The TF was prepared from blood donated by normal, healthy, lepromin skin test-positive individuals. During treatment all four of the LL patients, but not the BL patient, developed clinical reversal reactions. Histopathologically, skin biopsies in these four LL patients showed evidence of transformation of collections of multibacillary macrophages into paucibacillary epithelioid cells and giant cells. To our knowledge, this is the first histopahtologic documentation of reversal reactions occurring in polar LL. To the extent that reversal reactions are evidence of effective cell-mediated immunity of Mycobacterium leprae, these results indicate that TF is capable of at least partial correction of the immunologic deficit of lepromatous leprosy.

Publication Types:
• Case Reports

PMID: 717642 [PubMed - indexed for MEDLINE]
Jpn J Surg. 1983 Jul;13(4):304-11. Related Articles, Links

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

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.

PMID: 6606065 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1979 Jan;35(1):45-52. Related Articles, Links

A placebo controlled clinical trial of transfer factor in lepromatous leprosy.

Faber WR, Leiker DL, Nengerman IM, Schellekens PT.

The effects of repeated injections of transfer factor over a period of 20 weeks were investigated in fourteen bacteriologically positive patients at the lepromatous side of the leprosy spectrum. All patients showed negative (0 mm induration) skin tests to M. leprae antigens (i.e. leprolin and lepromin). Of these patients, seven were treated with transfer factor with a total of 9 units (1 unit being equivalent to 5 x 10(8) lymphocytes) and seven with a placebo. Maintenance treatment with clofazimine was continued. Transfer factor was prepared from the lymphocytes of donors who showed positive skin tests to M. leprae antigens (i.e. leprolin greater than or equal to 12 mm induration, average 15.5 mm or lepromin greater than or equal to 8 mm induration, average 13.6 mm), as well as a positive lymphocyte transformation in vitro to M. leprae (the average transformation being higher than the average transformation of lymphocytes of tuberculoid leprosy patients). No differences were found between the two groups as regards the clinical course of the disease, the histopathological and bacteriological evaluation of skin biopsies, changes in skin test reactivity to various antigens (i.e. lepromin, leprolin, PPD, Mumps, C. albicans, Tr. rubrum and Varidase), as well as the lymphocyte transformation in vitro to various mitogens (i.e. PHA, PWM, Con A) and antigens (i.e. M. leprae, leprolin, PPD, BCG, Mumps, C. albicans, Trichophyton and Varidase). No evidence was found to suggest that transfer factor is a valuable adjuvant in the treatment of lepromatous leprosy patients or that it increases cell-mediated immune reactivity towards M. leprae.
Acta Derm Venereol. 1980;60(1):51-5. Related Articles, Links

Transfer factor in the treatment of chronic mucocutaneous candidiasis: a controlled study.

Mobacken H, Hanson LA, Lindholm L, Ljunggren C.

A controlled cross-over study with transfer factor was carried out on 7 patients suffering from chronic mucocutaneous candidiasis. Only one patient showed clinical improvement, which started during a period of pretreatment with 5-fluorocytosine given orally 14 days before the patient entered this trial. No conversion to a positive skin test with Candida antigen or PPD was demonstrated following TF in the 6 patients who were anergic to either of these antigens. Variations in the cell-mediated immune response as revealed by lymphocyte transformation were observed in most patients,

especially when studied over a long period of time. However, no pronounced efficacy of TF vis-a-vis placebo in normalizing the cell-mediated immune response could be demonstrated in the 5 patients who completed the clinical trial. Systemic side effects were not observed.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 6153834 [PubMed - indexed for MEDLINE]
Dermatologica. 1980;161(4):243-9. Related Articles, Links

Transfer factor treatment in bullous pemphigoid. Impaired T cell function.

Khan A, Ayyar R, Michaelson JD, Weaver RE, Hill NO.

A patient with bullous pemphigoid, not responding to prednisone, had impaired cellular immunity. Transfer factor (TF) was given in doses of 10 U/m2 intramuscularly to improve T cell immunity, at a frequency of 3 times to once a week. Clinical improvement fluctuated with changes in the frequency of TF injections. The skin has been clear of the lesions for the past 9 months. Her T cell functions became normal and serum IgE decreased from 900 U/ml to 270 U/ml. She has received a total of 1,732 U of TF. This report is intended to encourage investigation into T cell functions in patients with bullous pemphigoid and controlled trials of TF in this disease.

Publication Types:
• Case Reports

PMID: 6157579 [PubMed - indexed for MEDLINE]
1: Wien Klin Wochenschr. 1983 Oct 28;95(20):738-42. Related Articles, Links

[Transfer factor as adjuvant immunotherapy in invasive cervix cancer. Report of a double-blind study]

[Article in German]

Wagner G, Gitsch E, Havelec L, Knapp W, Rainer H, Selander S.

From 1977 to 1982 a prospective randomized double-blind study comparing transfer-factor (TF) versus placebo was conducted in invasive cervical cancer patients after radical surgery and irradiation. The husbands of the cancer patients were selected as leukocyte donors for TF preparations. 60 patients entered the study; 28 patients received placebo and 32 patients received TF. The comparability of both collectives was excellent concerning age and tumor stage. One patient treated with TF died intercurrently. The rate of recurrence of cancer was 5 in the 31 TF-treated patients and 11 in the 28 patients receiving placebo, which was significantly different (p less than 0,05). This difference was even greater when only patients treated for at least 3 months were compared (3 recurrences in the TF-group and 11 recurrences in the placebo-group). Further aspects of this clear clinical results are discussed.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 6362210 [PubMed - indexed for MEDLINE]
Wien Klin Wochenschr. 1983 Oct 28;95(20):738-42. Related Articles, Links

[Transfer factor as adjuvant immunotherapy in invasive cervix cancer. Report of a double-blind study]

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From 1977 to 1982 a prospective randomized double-blind study comparing transfer-factor (TF) versus placebo was conducted in invasive cervical cancer patients after radical surgery and irradiation. The husbands of the cancer patients were selected as leukocyte donors for TF preparations. 60 patients entered the study; 28 patients received placebo and 32 patients received TF. The comparability of both collectives was excellent concerning age and tumor stage. One patient treated with TF died intercurrently. The rate of recurrence of cancer was 5 in the 31 TF-treated patients and 11 in the 28 patients receiving placebo, which was significantly different (p less than 0,05). This difference was even greater when only

patients treated for at least 3 months were compared (3 recurrences in the TF-group and 11 recurrences in the placebo-group). Further aspects of this clear clinical results are discussed.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 6362210 [PubMed - indexed for MEDLINE]
1: Acta Neurol Scand Suppl. 1977;63:123-31. Related Articles, Links

Cell-mediated immunity in multiple sclerosis.

Espinoza LR, Ebers G, Mountcastle W, Zabriskie JB.

The blastogenic response of MS lymphocytes to a group of paramyxovirus antigens and to phytohemagglutinin was investigated. Comparative studies were performed in a selected group of patients before and after transfer factor therapy. There was no blastogenic response of lymphocytes to the paramyxovirus antigens tested in MS patients and normal controls, as measured by the incorporation of 14C thymidine. The stimulation index was below 2.5 even after transfer factor therapy. Lymphocyte transformation induced by PHA appeared significantly depressed in the MS patient group before transfer factor therapy when compared with the normal control group. The presence of serum factors that may depress PHA-induced lymphocyte transformation were looked for and not found. Following transfer factor therapy, an increase of the PHA response was observed in the MS group, such that a statistically significant difference in response compared with the normal control group was no longer present.

PMID: 265663 [PubMed - indexed for MEDLINE]
Acta Derm Venereol. 1982;62(1):47-53. Related Articles, Links

Transfer factor therapy in mycosis fungoides: a double-blind study.

Thestrup-Pedersen K, Grunnet E, Zachariae H.

Sixteen patients with mycosis fungoides (MF) were given either active transfer factor (TF) or heat-inactivated TF as additional therapy to topical nitrogen mustard or PUVA. The TF was prepared from non-selected healthy blood donors. The clinical evaluation after 2 years of therapy showed that among 8 patients treated with active TF, none went into complete remission of their disease 4 patients had partial remission, one was unchanged, 2 progressed, and one died of active MF. In the placebo-treated group, 5 patients achieved complete remission and 2 partial remission. One patient died early in the trial due to cardiac disease. Immunological studies during the first year of therapy revealed cutaneous anergy towards tuberculin in most patients. This anergy did not change during TF therapy and differed from normal lymphocyte reactivity in vitro after tuberculin stimulation. At the start of treatment the patients had diminished levels of T lymphocytes in peripheral blood. A temporary increase was observed in the total number of T lymphocytes in patients after one month of treatment with active TF. After one year the T lymphopenia had disappeared in both groups. The mitogen reactivity of lymphocytes was found to be normal (PHA, PWM) or somewhat reduced (Con A). It is concluded that under the conditions employed in this trial, TF was not able to prevent progression of early mycosis fungoides, when viewed over a period of 2 years.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial
• Randomized Controlled Trial

PMID: 6175137 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):175-85. Related Articles, Links

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

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.

Publication Types:
• Clinical Trial

PMID: 8993778 [PubMed - indexed for MEDLINE]
Acta Derm Venereol. 1975;55(3):187-90. Related Articles, Links

Lymphocyte transformation, IgE and T-cells in eczema vaccinatum treated with transfer factor. A case report.

Dahl B, Thestrup-Pedersen K, Ellegaard J, Zachariae H.

Transfer factor (TF) was given to intensify the cell-mediated immune reactions in an atopic patient with generalized vaccinia. The patient showed marked reactivity of peripheral blood lymphocytes to stimulation with phytohaemagglutinin and pokeweed mitogen, but also in nonstimulated cultures. However, later tests with mitogen stimulation of lymphocytes indicated a defective cellular defence mechanism. The addition of autologous plasma to lymphocyte cultures depressed the reactivity of PHA-stimulation considerably. Initially, the patient also showed a normal T-lymphocyte count in peripheral blood, but six months after her vaccinia, extremely high serum IgE levels and a decreased percentage of T-lymphocytes was observed. Although an evaluation of the clinical effect of transfer factor injection is difficult, it should be noted that the patient's temperature immediately fell to normal, and her general health improved following treatment.

PMID: 50689 [PubMed - indexed for MEDLINE]

Allergy. 1981 Feb;36(2):99-105. Related Articles, Links

Influence of dialysable transfer factor on IgE concentrations in patients with atopic dermatitis.

Jarisch R, Eibl M, Sandor I, Boltz A.

Dialysable transfer factor (TF) was given in 10 paediatric patients with severe atopic dermatitis (AD). Ten patients with AD, matched for age and severity of disease, served as controls. Prior to the therapy with TF and at weekly intervals thereafter, T- and B-cells in the blood, PHA-stimulation, total IgE and specific IgG antibodies to inhalant and food antigens were determined. Therapy with TF was followed by IgE depression in 8/10 patients and was most pronounced in three patients with initially high levels. Some decrease of IgE levels was seen in four controls also, none of them, however, fell to normal levels as was seen in two of the treated patients. Specific IgE levels decreased slightly, but always remained within the pathological range. T-cell counts in the blood increased in 2/10 cases as well as PHA-stimulation, B-cells counts remained within normal limits. Clinical improvement was seen in one patient, five improved slightly and four remained unchanged. Our results indicate, that transfer factor can lower total IgE levels in cases with atopic dermatitis. The effect is most marked in patients with high total IgE levels. Skin involvement, however, does not closely follow in vitro findings.

PMID: 6972179 [PubMed - indexed for MEDLINE]
Acta Allergol. 1977 Aug;32(4):236-7. Related Articles, Links

Long-term transfer factor treatment in severe atopic dermatitis.

Thulin H, Ellegaard J, Thestrup-Pedersen K, Zachariae H.

Transfer factor therapy was applied in three patients with severe atopic dermatitis and given at regular intervals for 1 1/2 years. Clinically, slight improvements were seen, attacks of impetigo ceased and admissions to hospital were not necessary. However, IgE concentrations in serum remained constantly high in all cases and the absolute number of T and B lymphocytes was continuously subnormal despite treatment. The in vitro cellular reactivity to PPD as assayed by a leucocyte migration test was not significantly altered in the patients, although a slight increase was found early on in the therapy. Finally, a serum factor inhibiting leucocyte migration and appearing simultaneously with attacks of impetigo

disappeared during treatment. In conclusion, no convincing effect of transfer factor therapy was encountered in immune parameters and no major alterations were found in the status of the patients' atopic dermatitis.

PMID: 578361 [PubMed - indexed for MEDLINE]
Rev Alerg Mex. 2003 Jan-Feb;50(1):3-7. Related Articles, Links

[Lymphocyte apoptosis in atopic dermatitis treated with transfer factor]

[Article in Spanish]

Garcia Angeles J, Flores Sandoval G, Orea Solano M, Serrano E, Estrada Parra S.

Departamento de Alergia e Inmunologia Clinica, Hospital Regional Lic. Adolfo Lopez Mateos, ISSSTE, Av. Universidad 1321, col. Florida, CP 01030, Mexico, DF.

BACKGROUND: Atopic dermatitis is an inflammatory dysfunction in whose physiopathology the lymphocytes T play an important role in the regulation of the inflammatory process. OBJECTIVE: To determine and to characterize the role of apoptosis of lymphocytes in patients with moderate to severe atopic dermatitis before and after treatment with transfer factor. MATERIAL AND METHODS: Fifteen patients with moderate to severe atopic dermatitis in a range of age from 5 to 45 were included in the study. Fifteen healthy subjects were taken as a control group. In all subjects it was determined the apoptosis of the lymphocytes by means of annexin and TUNEL techniques, as well as the expression of CD95 cells. The 15 patients with atopic dermatitis received treatment with transfer factor in stepped dose as follows: 1 U/day/5 doses, 1 U/week/3 doses, 1 U/15 days/2 doses, 1 U/30 days, until completing three months. At the end of this period new determinations were done to measure apoptosis of lymphocytes and PMN. At the beginning and at the end assessments of the severity in relation to the scale SCORAD were made. RESULTS: By means of both techniques no significant difference was found in the percentage of apoptotic lymphocytes between patients and control subjects. Differences of the expression of CD95 between patients and control subjects before and after treatment were not significant. There was a significant difference ($p < 0.01$) of severity from the beginning to the end of treatment with transfer factor in patients with atopic dermatitis. CONCLUSION: No significant differences of apoptosis of lymphocytes were found in patients with atopic dermatitis who received treatment and control subjects, neither before not after the treatment with transfer factor. It was verified the decrease in the severity of the symptoms related to the treatment with transfer factor.

PMID: 12822541 [PubMed - indexed for MEDLINE]
Acta Derm Venereol. 1978;58(6):497-500. Related Articles, Links

Failure of transfer factor therapy in atopic dermatitis.

Hovmark A, Ekre HP.

A controlled clinical study was conducted on 6 patients with atopic dermatitis to assess the efficacy of transfer factor. After the code was broken the 3 patients treated with placebo preparation were treated with transfer factor for a further period of 10 weeks. No definite therapeutic effects could be demonstrated. The immunological in vivo and in vitro tests failed to reveal any effects except for a change to positive in the tuberculin skin test in those patients who had previously been skin test negative. The treatment had to be discontinued in one patient due to a suspected allergic reaction against transfer factor.

Publication Types:
• Case Reports
• Clinical Trial
• Controlled Clinical Trial

PMID: 83072 [PubMed - indexed for MEDLINE]
Rev Alerg Mex. 2001 Mar-Apr;48(2):56-64. Related Articles, Links

[Comparative treatment between thalidomide and transfer factor in severe atopic dermatitis]

[Article in Spanish]

Sosa M, Flores G, Estrada S, Orea M, Gomez Vera J.

Servicio de alergia e inmunologia clinica, Hospital Regional Lic. Adolfo Lopez Mateos, ISSSTE, Av. Universidad 1321-colonia Florida 01030 Mexico, DF.

AIMS: The atopic dermatitis is an chronic inflammatory illness of the skin. It exists an interrelation complex of factors gene, environmental, and psychological that contribute to the development and severity of the illness. The immunol aberrations significant is the answer increased of IgE specific antibodies toward antigens common, the liberation is increased of immunol mediators by the basophils and mast cells, eosinophils peripheral and local, besides enlarges the biphasic activity Th1/Th2 with liberation of cytokines (IL-4, IL-5, IL-13), GM-C5F, and decrease of IFN-gamma by the cells Th1. Leung to report a knowledge upon the bases immunopathologies of it atopic dermatitis has immunopathologies clinical important for the diagnosis and processing. Alternatives multiples of processing by the same complexity of the illness exist. OBJECTIVE: To compare the security and the clinical efficacy of the thalidomide and the factor of transfer in the atopic dermatitis severe. MATERIAL AND METHOD: Were studied patient with diagnosis of atopic dermatitis severe in agreement with the criterions of Hanifin and Rajka that they entered to the service of Allergy and Immunology Clinical of the Hospital Regional Lic. Adolfo Lopez Mateos (public hospital). They were included 19 patient (women 12 and men 7, with age average 30 +/- 4 years). They were distributed in two groups. The first group of 5 patient administration thalidomide 200 mg/d during six months. The second group am administered the factor of transfer a total of 15 units by road oral during six months. Studies of laboratory for appraisal were requested immunology and metabolic pretreatment and pretreatment. RESULTS: In the group A dealt with thalidomide 5 patient and the group B dealt with FT, both presented a statistically significant decrease, as for the extension of the wounds ($p < 0.01$), and 1 am observed greater reduction in the intensity of the symptoms, the SCORAD total ($p < 0.001$ and $p < 0.001$ respectively) with statistical difference among them. None presented alterations immunologies and metabolic secondary to the use of the two drugs and not there was the need to suspend the processing. During the period of study, the patient were maintained controlled to the allergic rhinitis and the asthma. DISCUSSION: In the atopic dermatitis by its secondary clinical complexity to the multifactors etiologic, the alternatives of processing utilized in the present study are an option the security and efficacy, I am observed better clinical.

Publication Types:
• Clinical Trial

PMID: 11421176 [PubMed - indexed for MEDLINE]
Cancer. 1988 Apr 15;61(8):1543-9. Related Articles, Links

A randomized, double-blind, placebo-controlled trial of transfer factor as adjuvant therapy for malignant melanoma.

Miller LL, Spitler LE, Allen RE, Minor DR.

Paul M. Aggelar Memorial Laboratory, Children's Hospital of San Francisco, California.

One hundred and sixty-eight evaluable patients participated in a randomized, double-blind study of transfer factor (TF) versus placebo as surgical adjuvant therapy of Stage I and Stage II malignant melanoma. Eighty-five patients received TF prepared from the leukocytes of healthy volunteer donors; eighty-three participants received placebo. Therapy was initiated within 90 days of resection of all evident tumor and continued until 2 years of disease-free survival or the occurrence of unresectable dissemination of melanoma. Known prognostic variables were similarly distributed in the treatment and control groups, documenting the randomization efficacy. Three endpoints were analyzed: disease-free interval, time to Stage III metastasis, and survival. After a median follow-up period of 24.75 months, there was a trend in favor of the placebo group with regard to all three endpoints and this was significant (P less than or equal to 0.05) for time to Stage III metastasis. These findings indicate that TF is not effective as surgical adjuvant therapy of malignant melanoma.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 3280114 [PubMed - indexed for MEDLINE]
Cancer. 1983 Jan 15;51(2):269-72. Related Articles, Links

Randomized controlled trial of transfer factor in Stage II malignant melanoma.

Bukowski RM, Deodhar S, Hewlett JS, Greenstreet R.

Thirty-six patients with Stage II malignant melanoma were randomized to no further therapy or transfer factor (TF) following surgical removal of all evident disease. Eighteen patients received TF, and 18 were in the surgery only group. Median disease-free intervals were 12.0 and 10.0 months, and survival, 40.8 and 27.0 months, respectively. Nine TF patients and four control patients remain alive. These differences were not statistically significant, and no adjuvant effect of TF could be demonstrated.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 6336977 [PubMed - indexed for MEDLINE]
Cancer. 1981 Mar 1;47(5):882-8. Related Articles, Links

Adjuvant immunotherapy of high risk stage I melanoma with transfer factor.

Blume MR, Rosenbaum EH, Cohen RJ, Gershow J, Glassberg AB, Shepley E.

Following conventional surgical management, 100 patients with high risk Stage I melanoma were treated with transfer factor to reduce the incidence of disease recurrence. All patients had primary lesions invasive to Clark's level III or deeper and exceeding 1.0 mm in measured thickness. Ninety-six patients are available for analysis at 15 to 67 months (median: 30 months) after diagnosis. Nine patients have had a recurrence of disease (treatment failure), and one has died. Actuarial non-failure rate is 90%, and survival rate is 99% at five years. A nonrandomized but contemporary control group of 46 patients displaying comparable risk factors was treated with surgery alone. The non-failure rate of this group is 63%, and the survival rate is 69%, data consistent with the results of several published studies. These results suggest that transfer factor immunotherapy may be a valuable adjunct in the treatment of patients with high risk Stage I melanoma.

Publication Types:
• Clinical Trial

PMID: 7013963 [PubMed - indexed for MEDLINE]

Cancer. 1980 Jan 1;45(1):57-63. Related Articles, Links

Adjuvant immunotherapy with transfer factor in patients with melanoma metastatic to lung.

Gonzalez RL, Wong P, Spitler LE.

Nine patients with resectable pulmonary metastases of malignant melanoma were treated with surgery and transfer factor. Twelve months after thoracotomy, all were alive. After a median follow-up of 20 months, only one patient had died. Historic, other-center controls treated with surgery alone had a significantly (p less than 0.025) lower survival rate. Recurrence rates tended to be lower in the transfer factor group, but the differences were not significant. These results suggest that transfer factor may prolong survival in patients with an immunologically responsive malignancy and a small residual tumor burden.

Publication Types:
• Clinical Trial

PMID: 6985827 [PubMed - indexed for MEDLINE]
Cancer. 1984 Aug 15;54(4):663-9. Related Articles, Links

Adjuvant immunotherapy of primary resected lung cancer with transfer factor.

Fujisawa T, Yamaguchi Y, Kimura H, Arita M, Baba M, Shiba M.

One hundred seventy-one patients were studied in order to evaluate the clinical efficacy of the transfer factor (TF) for primary resected lung cancers under a randomized controlled trial. Eligible cases for evaluation were randomly chosen at 75 and 74 patients in TF and control groups, respectively. The same long-term intermittent adjuvant chemotherapy was administered to two groups as a standard therapy. The distribution of clinical features in both groups was very similar. The overall survival rates of the TF group at 2 and 4 years postoperatively were 69% and 53%, respectively, which was about 15% better than the control group, but this difference could not yet be considered statistically significant. The survival of the TF group was significantly better than that of the control group in patients with Stages I + II or curative resection (P less than 0.05 by Cox-Mantel test); however, there was no significant difference in patients with Stages III + IV, or noncurative resection. The recurrence rate of pulmonary and mediastinal regions was less in the TF group. In conclusion, TF seems to suppress postoperative recurrence and appears to be beneficial for primary resected lung cancer patients, especially at early stages, as postoperative adjuvant immunotherapy.

Publication Types:
• Clinical Trial

PMID: 6378354 [PubMed - indexed for MEDLINE]
Jpn J Surg. 1984 Nov;14(6):452-8. Related Articles, Links

Randomized controlled trial of transfer factor immunochemotherapy as an adjunct to surgical treatment for primary adenocarcinoma of the lung.

Fujisawa T, Yamaguchi Y, Kimura H, Arita M, Shiba M, Baba M.

A total of 102 patients were studied in a randomized controlled trail to evaluate the clinical effect of transfer factor (TF) for primary resected adenocarcinoma of the lung. The TF and Control groups consisted of 50 and 52 randomly chosen patients, respectively. However, 6 and 5 patients were excluded from both groups for various reasons, therefore the total of cases eligible for evaluation were 44 and 47 in the TF and Control groups, respectively. The clinical features of both groups were similar. The survival of the TF group was significantly better than that of Controls in Stage I cases (p less than 0.05), however, there was no significant difference in patients in Stages II, III and IV. Significant differences were found between the TF and Control groups in curative resection cases (p less than 0.05), however, no significant difference was seen in either the relatively curative resection or noncurative resection groups. TF seems to inhibit postoperative recurrence and appears to be an effective postoperative adjuvant immunotherapeutic for primary resected adenocarcinoma of the lung, especially at the relatively early stages.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 6397652 [PubMed - indexed for MEDLINE]
Gan No Rinsho. 1983 Oct;29(12):1409-16. Related Articles, Links

[Transfer factor immunochemotherapy for primary lung cancer--evaluation of histologic types]

[Article in Japanese]

Fujisawa T, Yamaguchi Y.

The clinical effect of leucocyte dialysate, including Transfer Factor (TF), on different histologic types of primary resected lung cancer was studied. This TF immunotherapy protocol included 171 patients. Eligible cases for evaluation were randomly chosen; the TF group and control group consisted of 75 and 74 patients, respectively. The TF group included 40 adenocarcinomas, 29 epidermoid carcinomas and 6 other histologic types of carcinoma. The control group included 42 adenocarcinomas, 25 epidermoid carcinomas and 7 other histologic types of carcinoma. The distribution of clinical features in the TF and control group was very similar, not only in adenocarcinoma but also in epidermoid carcinoma. The postoperative follow-up term was 2 to 55 months in both groups. Survival in the TF group of patients with adenocarcinoma of stages I + II or curative resection was significantly better than in the control group (p less than 0.005, Cox-Mantel test). There was no significant intergroup difference in patients with stages III + IV, relative curative or noncurative resection. Survival in the TF group of patients with epidermoid carcinoma of stages I + II or III + IV was about 20% better than in the control, however, there was no significant difference between the 2 groups. On the other hand, survival in the TF group of patients undergoing relative curative resection was significantly better than in the control (p less than 0.005, Cox-Mantel test). There was no significant difference among patients who underwent curative or noncurative resection. Time-versus-recurrence curves were evaluated by the Kaplan-Meier method; there was a significant difference between patients with stages I + II, but not between patients with stages III + IV. The frequency of recurrence of regional or intrapulmonary distant metastasis was lower in the TF group. It is suggested that TF suppresses postoperative recurrence and that it may be beneficial as postoperative adjuvant immunochemotherapy in primary resected lung cancer patients, especially those with relatively early stage cancer.

PMID: 6315989 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):117-21. Related Articles, Links

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

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.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 8993769 [PubMed - indexed for MEDLINE]

Ann Thorac Surg. 1984 Aug;38(2):140-5. Related Articles, Links

Transfer factor in the treatment of carcinoma of the lung.

Kirsh MM, Orringer MB, McAuliffe S, Schork MA, Katz B, Silva J Jr.

From 1976 to 1982, 63 patients with carcinoma of the lung underwent curative pulmonary resection, mediastinal lymph node dissection, and postoperative mediastinal irradiation when indicated. After operation, the patients were randomized by cell type and stage of disease into two groups. Beginning 1 month postoperatively, Group 1 patients (N = 28) received 1 ml of transfer factor that had been extracted from the blood of normal individuals. Subsequent doses were administered at 3-month intervals. Group 2 patients (N = 35) served as controls. There were no significant differences between the two groups with respect to age, sex, extent of resection, histological cell type, or stage of disease. Twenty of the 28 treated patients were alive and free from disease from 7 to 77 months after treatment, whereas 17 of the 35 control patients were free from disease. The 1-year survival for Group 1 was 84% and for Group 2, 81%. The 2-year survival was 78% for Group 1 and 46% for Group 2 (p = 0.045). The survival rates by stage of disease were as follows: Stage I, 15 out of 17 or 88% in Group 1 and 15 out of 23 or 65% in Group 2 (p = 0.097); Stages II and III, 5 out of 11 or 45% in Group 1 and 3 out of 12 or 25% in Group 2 (p = 0.304). The results of the study suggest that the administration of transfer factor to patients who have undergone pulmonary resection for carcinoma of the lung can have a significant impact on the prolongation of life.

Publication Types:
• Clinical Trial

PMID: 6380436 [PubMed - indexed for MEDLINE]
Ann Thorac Surg. 1992 Mar;53(3):391-6. Related Articles, Links

Adjuvant treatment using transfer factor for bronchogenic carcinoma: long-term follow-up.

Whyte RI, Schork MA, Sloan H, Orringer MB, Kirsh MM.

Section of Thoracic Surgery, University of Michigan, Ann Arbor.

Transfer factor, a dialyzable lymphocyte extract that may act as an immune stimulator by transferring antigen-specific immunity between genetically dissimilar individuals, was administered in a prospective, randomized study to patients with non-small cell bronchogenic carcinoma. Between 1976 and 1982, 63 patients who underwent pulmonary resection, mediastinal lymph node dissection, and, when indicated by the presence of mediastinal lymph node involvement, mediastinal irradiation were randomized into two groups. Group 1 (n = 28) received 1 mL of pooled transfer factor at 3-month intervals after operation; group 2 (n = 35) served as controls and received saline solution. There were no statistically significant differences between the two groups with respect to age, sex, tumor histology, stage of disease, or extent of resection. One patient was lost to follow-up at 96 months; follow-up was complete in all others through July 1990. In patients receiving transfer factor, the 2-, 5-, and 10-year survival rates were 82%, 64%, and 43% respectively, whereas in controls they were 63%, 43%, and 23%. Survival in patients receiving transfer factor was consistently better than in those receiving placebo. Furthermore, survival in patients receiving transfer factor was greater at all stages of disease for both adenocarcinoma and squamous cell carcinoma. Although these long-term results were not statistically significant using survival analysis with covariates (p = 0.08), they confirm our previously reported short-term findings suggesting that administration of transfer factor, either through nonspecific immune stimulation, enhancement of cell-mediated immunity, or an as yet undefined mechanism, can improve survival in patients with bronchogenic carcinoma.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 1540053 [PubMed - indexed for MEDLINE]
J Exp Pathol. 1987 Summer;3(4):565-8. Related Articles, Links

Transfer factor adjuvant therapy in nonsmall-cell lung carcinoma. (NSCLC) after surgery and radiotherapy.

Busutti L, Blotta A, Mastrorilli M, Savorani GC, Pizza G, De Vinci C.

Department of Radiotherapy, Malpighi-S. Orsola Hospital, Bologna, Italy.

PMID: 2842483 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):109-15. Related Articles, Links

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

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.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 8993768 [PubMed - indexed for MEDLINE]
Cancer Res. 1976 Feb;36(2 pt 2):720-3. Related Articles, Links

In vivo and in vitro studies of immunotherapy of nasopharyngeal carcinoma with transfer factor.

Goldenberg GJ, Brandes LJ.

Epstein-Barr virus, the apparent cause of infectious mononucleosis, may also be an etiological agent in nasopharyngeal carcinoma and Burkitt's lymphoma. Lymphocytes from normal individuals with anti-Epstein-Barr virus antibody activity may be sensitized to Epstein-Barr virus and contain transfer factor with the potential to program and/or recruit other lymphocytes to react against the virus and/or viral antigens. A patient with nasopharyngeal carcinoma refractory to conventional therapy was treated with transfer factor obtained from normal, young adults with previous history of infectious mononucleosis. Following immunotherapy, apparent slowing of tumor growth was observed, which was associated with intense lymphocytic infiltration of the tumor and reconstitution of delayed cutaneous hypersensitivity reactions to microbial recall antigens. A double-blind randomized clinical trial has been initiated to determine whether transfer factor immunotherapy is a useful adjunct to radiotherapy in the primary treatment of patients with nasopharyngeal carcinoma. If successful, a similar trial might be considered for African patients with Burkitt's lymphoma.

Publication Types:
• Case Reports
• Clinical Trial
• Randomized Controlled Trial

PMID: 1253157 [PubMed - indexed for MEDLINE]
Anticancer Res. 1990 Sep-Oct;10(5A):1183-7. Related Articles, Links

Specific transfer factor with activity against Epstein-Barr virus reduces late relapse in endemic Burkitt's lymphoma.

Neequaye J, Viza D, Pizza G, Levine PH, De Vinci C, Ablashi DV, Biggar RJ, Nkrumah FK.

University of Ghana School of Medicine, Accra.

Twenty-seven children with abdominal Burkitt's lymphoma (stage III), who had achieved complete remission, were entered into a prospective controlled trial of adjunct treatment with Epstein-Barr virus (EBV)-specific transfer factor (TF). Two patients treated with TF and 2 controls relapsed early (less than or equal to 12 weeks). Two out of 12 TF-treated patients and 5 out of 11 controls subsequently suffered relapses. Time to first late relapse was longer among TF-treated patients ($p = 0.08$), and no late relapse occurred while a patient was receiving TF treatment. Thus it seems that specific TF might be useful in the management of endemic Burkitt's lymphoma and also in the treatment of other virus-associated cancers and diseases.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 2173470 [PubMed - indexed for MEDLINE]
Exp Pathol. 1987 Summer;3(4):463-9. Related Articles, Links

Transfer factor in prevention of Burkitt's lymphoma relapses.

Nkrumah FK, Pizza G, Neequaye J, Viza D, De Vinci C, Levine PH.

Burkitt Tumour Project, Univ. of Ghana Medical Sch. Accra.

Twenty-two African children with endemic Burkitt's lymphoma entered a study to evaluate the possible efficacy of a transfer factor (TF) with specific activity against Eptein-Barr virus in preventing disease relapses. Five of eleven patients have so far relapsed in the non TF-treated group as against two of eleven in the TF-treated group. The patterns of relapse and observable increased disease free remission duration in the TF-treated group strongly suggest a beneficial effect particularly in the prevention of late relapses. A larger series of patients treated with this specific TF are needed to confirm these observations in endemic Burkitt's lymphoma.

PMID: 2842479 [PubMed - indexed for MEDLINE]
Biotherapy. 1994;8(1):63-8. Related Articles, Links

Transfer factor prevents relapses in herpes keratitis patients: a pilot study.

Pizza G, Meduri R, De Vinci C, Scorolli L, Viza D.

Immunodiagnosis and Immunotherapy Unit, S. Orsola-Malpighi Hospital, Bologna, Italy.

Transfer Factor is a dialysable moiety obtained from immune lymphocytes. It has been successfully used for the treatment of several viral infections including labial and genital herpes. In the present study, thirty-three patients with low immune response to HSV antigens and suffering from herpes ocular infections were orally treated with HSV-specific transfer factor (TF). Their relapse index was reduced from 20.1 before treatment to 0.51 after TF administration, with only 6/33 patients relapsing. Although this is not a placebo-controlled-randomized study, the results suggest that TF specific for HSV antigens may be efficacious for preventing relapses of ocular herpes infections as has been the case with genital and labial localisations.

Publication Types:
• Clinical Trial

PMID: 7547082 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):61-6. Related Articles, Links

Efficacy of transfer factor in treating patients with recurrent ocular herpes infections.

Meduri R, Campos E, Scorolli L, De Vinci C, Pizza G, Viza D.

Eye Physiopathology Clinical Service, University of Bologna, Italy.

Recurrent ocular herpes is an insoluble problem for the clinician. As cellular immunity plays an important role in controlling herpes relapses, and other studies have shown the efficacy of HSV-specific transfer factor (TF) for the treatment of herpes patients, an open clinical trial was undertaken in 134 patients (71 keratitis, 29 kerato-uveitis, 34 uveitis) suffering from recurrent ocular herpetic infections. The mean duration of the treatment was 358 days, and the entire follow-up period 189,121 before, and 64,062 days after TF treatment. The cell-mediated immune response to the viral antigens, evaluated by the lymphocyte stimulation test (LST) and the leucocyte migration test (LMT) ($P < 0.001$), was significantly increased by the TF treatment. The total number of relapses was decreased significantly during/after TF treatment, dropping from 832 before, to 89 after treatment, whereas the cumulative relapse index (RI) dropped, during the same period, from 13.2 to 4.17 ($P < 0.0001$). No side effects were observed. It is concluded that patients with relapsing ocular herpes can benefit from treatment with HSV-specific TF.

Publication Types:
• Clinical Trial

PMID: 8993759 [PubMed - indexed for MEDLINE]

Biotherapy. 1996;9(1-3):67-72. Related Articles, Links

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

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.

PMID: 8993760 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):133-8. Related Articles, Links

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

De Vinci C, Pizza G, Cuzzocrea D, Menniti D, Aiello E, Maver P, Corrado G, Romagnoli P, Dragoni E, LoConte 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.

Publication Types:
• Clinical Trial

PMID: 8993771 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):97-103. Related Articles, Links

Transfer factor in chronic mucocutaneous candidiasis.

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.

Publication Types:
• Clinical Trial

PMID: 8993766 [PubMed - indexed for MEDLINE]
Eur J Pediatr. 1984 Nov;143(1):45-8. Related Articles, Links

Immunological observations before and after successful treatment of chronic mucocutaneous candidiasis with ketoconazole and transfer factor.

Corbeel L, Ceuppens JL, Van den Berghe G, Claeys H, Casteels-Van Daele M.

A girl, 13 months of age, presented with generalised granulomatous skin, hair and mucosal candidiasis. Her lymphocytes failed to respond in vitro to Candida antigen (CA); the intradermal test with CA was also negative. Serum immunoglobulins, complement components, granulocyte functions (phagocytic and fungicidal), T-cell subsets, mitogenic and allogenic lymphocyte stimulation, natural killer cell activity and immune interferon production were all found to be normal. No circulating immune complexes were detected. Ketoconazole, an antimycotic drug, 5 mg/kg twice daily for 1 month and 2.5 mg/kg twice daily for another month spectacularly cleared all lesions. Afterwards, 4-monthly injections with transfer factor (TF) were given. Intradermal reactivity to CA was observed after the second TF injection. The lymphocyte responsiveness to CA in vitro became strongly positive 3 months after the last TF injection. The level of CA precipitins in serum, which was very high (11 lines) before ketoconazole treatment, decreased to 4 lines. No serum inhibitor of lymphocyte proliferation to CA could be demonstrated in the patient's serum before or after treatment. This specific CA unresponsiveness was not due to an excess of OKT8 + (suppressor) cells; macrophage migration inhibiting factor (MIF) production was normal. The nonresponsiveness might be due to antigenic overload or to suppressor cell induction not demonstrable in the present studies. The child has remained free of lesions during 3 years of follow-up without any further treatment.

Publication Types:
• Case Reports

PMID: 6096150 [PubMed - indexed for MEDLINE]
Z Gesamte Inn Med. 1986 Apr 1;41(7):214-6. Related Articles, Links

[Chronic mucocutaneous candida mycosis (CMCC) caused by a T-cell defect]

[Article in German]

Rytter M, Schonborn C, Lohrisch I, Haustein UF.

It is reported on a 42-year-old book-keeper with the granulomatous variant of the chronic mucocutaneous candidiasis which could be followed up for 28 years. The intensive systemic treatment with nystatin, 5-fluorocytosin and miconazol combined with the subcutaneous injection of transfer-factor and the local application of ointments containing nystatin and

clotrimazol did not only lead to the complete clearing of the lesions (4 years without any relapse), but also to the normalization of the T-lymphocyte count and the reconstitution of the formerly negative delayed type skin reactivity to candidin.

Publication Types:
• Case Reports

PMID: 3521108 [PubMed - indexed for MEDLINE]
Eur J Clin Microbiol Infect Dis. 1989 May;8(5):448-56. Related Articles, Links

Chronic mucocutaneous candidiasis.

Kirkpatrick CH.

Department of Medicine, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.

Chronic mucocutaneous candidiasis can be defined as a group of syndromes that have as a common feature infections of the skin, nails and mucous membranes with Candida albicans. A variety of disorders including endocrine dysfunctions, alopecia, vitiligo, malabsorption syndromes, neoplasms and other infections may also occur in patients with chronic mucocutaneous candidiasis, but these vary considerably from patient to patient. In most patients with chronic mucocutaneous candidiasis, there are abnormalities of cell-mediated immunity. These may be limited to antigens of Candida albicans, but in some patients they are more extensive and involve the T-lymphocyte-mediated responses to all antigens. These immunologic defects are the factors that predispose patients to infections with opportunistic organisms such as Candida spp. Fungal infections in patients with chronic mucocutaneous candidiasis usually respond to treatment with conventional antifungal agents, but often relapse shortly after treatment is stopped unless the defects in the cell-mediated immune system have been corrected.

Publication Types:
• Review
• Review, Tutorial

PMID: 2502409 [PubMed - indexed for MEDLINE]
Br J Dermatol. 1976 Jan;94(1):79-83. Related Articles, Links

Chronic mucocutaneous candidiasis treated with transfer factor.

Sousa MD, Cochran R, Mackie R, Parratt D, Arala-Chaves M.

A patient with chronic mucocutaneous candidiasis resistant to all tropical therapy has had extensive tests of immunological function carried out before and after administration of transfer factor. Immunological testing has been both specific, directed at responses to candida antigen, and non-specific, directed at general assessment of the patient's immune status. Transfer factor has been administered on three occasions in the past year. After each treatment temporary clinical improvement accompanied by changes in both specific and non-specific immunological responses have been observed. The possible mode of action of transfer factor in this case is discussed.

Publication Types:
• Case Reports

Allergol Immunopathol (Madr). 1976 Sep-Oct;4(5):345-50. Related Articles, Links

Clinical and immunological improvement in a patient with chronic mucocutaneous candidiasis treated with transfer factor.

Businco L, Aiuti F, Franchi F, Frati C, Cavalieri R, Rezza E.

In a 19 year old patient suffering from CMC since the first months of life, clinical improvement accompanied by correction of the immunologic defect was achieved by Transfer Factor therapy. After 12 months from the last administration of Transfer Factor the improvement persisted. The positive outcome of the treatment in this disease is not constant. Possibly only patients with cellular immunologic defects are susceptible of a favourable response, moreover it is thinkable that the quality of Transfer Factor and the dosage administered must play a role.

Publication Types:
• Case Reports

PMID: 1087530 [PubMed - indexed for MEDLINE]

Clin Exp Immunol. 1976 Mar;23(3):414-28. Related Articles, Links

Reconstitution of defective cellular immunity with foetal thymus and dialysable transfer factor. Long-term studies in a patient with chronic mucocutaneous candidiasis.

Kirkpatrick CH, Ottenson EA, Smith TK, Wells SA, Burdick JF.

Extensive studies of a 9-year-old boy with recurrent pulmonary infections and chronic mucocutaneous candidiasis disclosed a severe defect in cell-mediated immunity but normal humoral immune responses. These immunological defects were not improved by initial treatment with transfer factor. After receiving a foetal thymus transplant the patient developed positive delayed-type skin tests, could be sensitized with chlorodinitrobenzene, and showed progressive improvement of in vitro lymphocyte functions including spontaneous formation of rosettes with sheep erythrocytes and positive responses to phytohaemagglutinin, concanavalin A and allogeneic leucocytes. Moreover, lymph node cellularity increased, especially in the thymus-dependent zones. Though the in vitro responses persisted for over 1 year, skin tests became unreactive at 38 weeks. However, in contrast to the pre-transplant experience transfer factor was now effective in inducing positive skin tests. These studies provide a chronological account of the effect of the thymus on expression of lymphocyte-mediated immune responses in man and suggest that thymus-derived cells are required for acquisition of transfer factor-induced cellular immunity.

PMID: 947642 [PubMed - indexed for MEDLINE]
Adv Pediatr. 1980;27:89-115. Related Articles, Links

Transfer factor and its clinical application.

Schulkind ML, Ayoub EM.

Publication Types:
• Review

PMID: 7013447 [PubMed - indexed for MEDLINE]
Minerva Med. 1979 May 26;70(25):1773-85. Related Articles, Links

[A new approach to immunotherapy: the transfer factor]

[Article in Italian]

Di Padova F.

The transfer factor is a tiny molecule capable of transferring the function of the T lymphocytes (immunological memory and retarded hypersensitivity) from a sensitized to a non-sensitized individual. The exact structure and action modalities of the molecule have not yet been precisely established. The difficulties involved in the study of the transfer factor are aggravated by the lack of any suitable experimental model. The attention of immunologists is attracted by this factor which opens up new prospects for the treatment of cancer, immunological deficiencies and certain infectious and autoimmune diseases. More profound research would appear useful to evaluate if and in what cases a potentiation of the immune mechanism can represent an alternative to immunosuppression.

Publication Types:
• Review

PMID: 379697 [PubMed - indexed for MEDLINE]
Biomedicine. 1973 May;18(3):220-7. Related Articles, Links

Transfer factor therapy in immuno-deficiencies.

Griscelli C, Revillard JP, Betuel H, Herzog C, Touraine JL.

PMID: 4742861 [PubMed - indexed for MEDLINE]

Dtsch Med Wochenschr. 1973 Mar 2;98(9):446-51. Related Articles, Links

[Immune function and transfer factor]

[Article in German]

Grob PJ, Blaker F, Schulz KH.

Publication Types:
• Review

PMID: 4570866 [PubMed - indexed for MEDLINE]
Schweiz Med Wochenschr. 1974 Jan 26;104(4):146-7. Related Articles, Links

[Transfer factor therapy. Preliminary report]

[Article in German]

Francke C, Grob PJ.

PMID: 4811475 [PubMed - indexed for MEDLINE]
Ann Med Interne (Paris). 1972 Dec;123(12):1069-72. Related Articles, Links

[Specific immunotherapy using cell-mediated immune transfer factor. Preliminary results with semi-purified transfer factor]

[Article in French]

Berthaux P, Moulias R, Goust JM, Reinert P, Fournel JJ.

PMID: 4664543 [PubMed - indexed for MEDLINE]

[Transfer factor of cellular immunity. Preliminary therapeutic trials during specific immunologic deficiencies of an antigen in human clinical practice]

[Article in French]

Moulias R, Goust JM, Reinert P, Fournel JJ, Deville-Chabrolle A, Duoung N, Muller-Berat CN, Berthaux P.

PMID: 4357775 [PubMed - indexed for MEDLINE]
: Nouv Presse Med. 1973 May 19;2(20):1341-4. Related Articles, Links

[Transfer factor of cellular immunity. Preliminary therapeutic trials during specific immunologic deficiencies of an antigen in human clinical practice]

[Article in French]

Moulias R, Goust JM, Reinert P, Fournel JJ, Deville-Chabrolle A, Duong N, Muller-Berat CN, Berthaux P.

PMID: 4351886 [PubMed - indexed for MEDLINE]
Dtsch Med Wochenschr. 1973 Mar 2;98(9):415-20. Related Articles, Links

[Immunological defence and transfer factor therapy in chronic mucocutaneous candidiasis]

[Article in German]

Blaker F, Grob PJ, Hellwege HH, Schulz KH.

PMID: 4691560 [PubMed - indexed for MEDLINE]

Prog Clin Immunol. 1974;2:69-100. Related Articles, Links

Therapeutic uses of transfer factor.

Hitzig WH, Grob PJ.

Publication Types:
• Review

PMID: 4217910 [PubMed - indexed for MEDLINE]
Allerg Immunol (Leipz). 1978;24(4):243-53. Related Articles, Links

[The current position of the transfer factor investigation (author's transl)]

[Article in German]

Schroder I.

This critical review has attempted to describe the current knowledge about the preparation and characterisation of transfer factor, the biological assays, and the tendency to therapy of patients with immunodeficiencies, chronic infectious diseases, and neoplastic diseases on the basic of results of the two last years. Hypotheses for the mechanism of functional activities of transfer factor are discussed.

Publication Types:
• Clinical Trial

PMID: 154287 [PubMed - indexed for MEDLINE]
Schweiz Med Wochenschr. 1974 Oct 26;104(43):1501-6. Related Articles, Links

[Transfer factor and its therapeutic use]

[Article in German]

Rosenthal M.

PMID: 4549135 [PubMed - indexed for MEDLINE]
Vox Sang. 1975;28(4):257-77. Related Articles, Links

Uses of transfer factor.

Basten A, Croft S, Kenny DF, Nelson DS.

Publication Types:
• Review

PMID: 804764 [PubMed - indexed for MEDLINE]
Adv Neurol. 1974;6:107-26. Related Articles, Links

Transfer factor in diseases of the central nervous system.

Graybill JR.

Publication Types:
• Review

PMID: 4614652 [PubMed - indexed for MEDLINE]
South Med J. 1974 Jul;67(7):837-40. Related Articles, Links

Biologic and clinical implications of transfer factor.

Mutz I, Lankford J, Humphrey GB.

Publication Types:
• Review

PMID: 4599982 [PubMed - indexed for MEDLINE]
Adv Immunol. 1969;11:195-266. Related Articles, Links

Transfer factor.

Lawrence HS.

Publication Types:
• Review

PMID: 4910774 [PubMed - indexed for MEDLINE]
Lancet. 1973 Jul 14;2(7820):79-80. Related Articles, Links

Transfer factor.

[No authors listed]

PMID: 4123626 [PubMed - indexed for MEDLINE]
Zh Mikrobiol Epidemiol Immunobiol. 1979 Apr(4):13-6. Related Articles, Links

[Role of the transfer factor in transplantation immunology]

[Article in Russian]

Sakharov PP, Kudrina GP.

Publication Types:
• Review

PMID: 375633 [PubMed - indexed for MEDLINE]
J Allergy Clin Immunol. 1975 Jun;55(6):411-21. Related Articles, Links

Properties and activities of transfer factor.

Kirkpatrick CH.

Although there is agreement that transfer factor endows skin test-negative subjects with the ability to develop the delayed allergic responses of the transfer factor donors, there is little direct information on the mechanism of this phenomenon or on the nature of the active components (s). This report reviews some of the known effects of transfer factor or immune responses and inflammation. It is concluded that transfer factor has multiple sites of action, including effects on the thymus, on lymphocyte-monocyte and/or lymphocyte-lymphocyte interactions, as well as direct effects on cells in inflammatory sites. It is also suggested that the "specificity" of transfer factor is determined by the immunologic status of the recipient rather than by informational molecules in the dialysates. Finally, it is proposed that many effects of transfer factor may be due to changes in intracellular cyclic nucleotide content, especially accumulation of cGMP, in immunologically reactive cells.

PMID: 48524 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1980 Mar;39(3):708-16. Related Articles, Links

Transfer factor: failure to transfer reactivity in normal human subjects.

Spitler LE.

Transfer factor was prepared from highly selected normal donors. One lot was made from donors strongly reactive to coccidioidin and negative to Dharmendra antigen in in vivo and in vitro testing. The other lot was made from donors without reactivity to coccidioidin and strongly reactive to Dharmendra. Aliquots of each lot were injected into eight normal recipients. Eight additional normal recipients were given placebo injections. Before and after injection, skin test reactivity and in vitro testing were evaluated by an individual who did not know which preparation the patient received. Changes in immunologic reactivity in subjects receiving transfer factor could not be distinguished from those in subjects receiving placebo. I conclude that transfer factor does not cause enhancement of immunologic reactivity in normal subjects. A well designed, critical study is needed to determine whether or not it does, in fact, cause enhancement of immunologic reactivity in patients with impaired cellular immune reactivity.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 7379334 [PubMed - indexed for MEDLINE]
Fiziol Zh. 1997;43(3-4):25-32. Related Articles, Links

[Human specific transfer factor to Staphylococcus aureus antigens]

[Article in Ukrainian]

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.

PMID: 9303798 [PubMed - indexed for MEDLINE]
Birth Defects Orig Artic Ser. 1975;11(1):449-56. Related Articles, Links

Transfer factor II: results of therapy.

Spitler LE, Levin AS, Fudenberg HH.

Transfer factor is a dialyzable extract of sensitized leukocytes, which transfers reactivity from skin test-positive donors to skin test-negative recipients. Transfer factor supplied by our laboratory has been used therapeutically to induce cellular immunity in 78 patients around the world. Many patients received multiple doses of transfer factor ranging from 1 unit given every 6 months for 3 years to 1 unit every week for 6 months to as much as 8 units per week for a brief period. A total of 299 units of transfer factor have been given. Diseases in which transfer factor appeared to cause improvement include the Wiskott-Aldrich syndrome, severe combined immunodeficiency disease, mucocutaneous candidiasis, chronic active hepatitis, coccidioidmycosis, dysgammaglobulinemia, Behcet disease, aphthous stomatitis, linear morphea, familial keratoacanthoma and malignancy.

PMID: 1096990 [PubMed - indexed for MEDLINE]
Birth Defects Orig Artic Ser. 1975;11(1):445-8. Related Articles, Links

Transfer factor I: methods of therapy.

Levin AS, Spitler LE, Fudenberg HH.

Transfer factor was first discovered by Lawrence in 1955, but was not used therapeutically until 1969 when we reported its use in a Wiskott-Aldrich patient. Since that time, it has been used in a wide variety of disorders related to defects in cellular immunity, infectious diseases, and malignant diseases. This report describes our experience with transfer factor. Report number I discusses rationale for patient selection, procedures for transfer factor therapy, procedures for monitoring the efficacy of therapy, untoward effects of therapy, and experience with transfer factor therapy in severe combined dual system deficiency disorder. The results of our study on transfer factor therapy indicate that it is capable of inducing a clinically acceptable level of cell-mediated immunity in approximately 50% of patients with a variety of immunodeficiency disorders. It also appears to be a useful adjunct to chemotherapy, and may possibly act synergistically with transplanted fetal thymocytes to produce a constantly regenerating specifically competent source of T lymphocytes, thereby obviating the need for bone marrow transplant for severe combined dual system deficiency disorder.

PMID: 1080060 [PubMed - indexed for MEDLINE]
Ann N Y Acad Sci. 1979;332:228-35. Related Articles, Links

Transfer factor in immunodeficiency diseases.

Spitler LE.

Results of therapeutic trials of transfer factor in a number of laboratories suggest clinical benefit and enhancement of immunological reactivity in patients with primary or secondary immunodeficiency diseases. Long term follow-up of 32 patients with the Wiskott-Aldrich syndrome suggested that transfer factor caused conversion of immunologic reactivity, apparent clinical benefit, and prolonged survival in some, but not in all patients. In 18 patients with disseminated (Stage III) malignant melanoma treated with surgery and transfer factor, survival was better than would ordinarily be expected for disseminated disease (78% with mean follow-up of 2 years). A randomized trial has been initiated which will answer the question of the efficacy of transfer factor as surgical adjuvant therapy in malignant melanoma. Studies in human subjects suggested that transfer factor does not cause enhancement of reactivity in normal subjects, when evaluated in a controlled, double-blind fashion. Similar controlled studies in immunodeficient patients are necessary to ascertain whether transfer factor does cause enhancement of immune responses in these patients. Based on these observations, a guinea pig model was developed in which transfer factor caused abrogation of tolerance to ABA-Tyrosine.

PMID: 119460 [PubMed - indexed for MEDLINE]

Am J Med. 1979 Jul;67(1):59-66. Related Articles, Links

Transfer factor therapy in the Wiskott-Aldrich syndrome. Results of long-term follow-up in 32 patients.

Spitler LE.

Thirty-two patients with the Wiskott-Aldrich syndrome have been treated with transfer factor provided by this laboratory. Apparent clinical benefit was observed in 44 per cent of them. The mean age of the patients who showed clinical benefit was significantly greater than that of the patients who showed no benefit. Conversion of immunologic reactivity correlated with clinical benefit. Thirteen of the patients who received transfer factor are alive, and 17 have died (43 per cent survival). Clinical benefit was correlated with survival. The median survival was greater than five years in the patients who showed clinical benefit, whereas it was 18 months in those who did not show clinical benefit. We conclude that transfer factor caused conversion of immunologic parameters, apparent clinical benefit and prolonged survival in some, but not all, patients with the Wiskott-Aldrich syndrome.

PMID: 463917 [PubMed - indexed for MEDLINE]
Br J Dermatol. 1978 May;98(5):567-71. Related Articles, Links

Wiskott-Aldrich syndrome with partial response to transfer factor.

Mackie RM, Alcorn MJ, Stevenson RD, Cochran T, McSween RN.

A male infant presented with dermatitis, purpura and susceptibility to bacterial infections. The clinical diagnosis of Wiskott-Aldrich syndrome was confirmed and after full immunological assessment, treatment with transfer factor was commenced. This has resulted in a rise in the platelet count and improvement in the bleeding tendency. This improvement in the haematological aspect of the disease has, however, been accompanied by exacerbations of the cutaneous lesions.

Publication Types:
• Case Reports

PMID: 656329 [PubMed - indexed for MEDLINE]
Folia Haematol Int Mag Klin Morphol Blutforsch. 1983;110(5):677-84. Related Articles, Links

[Discrepancy between the clinical and immunologic picture of in vitro diagnosis during transfer factor therapy in a patient with Wiscott-Aldrich syndrome]

[Article in German]

Schutt C, Eggers G, Schroder I, Kruse H, Schulz M, Blau HJ.

The attempt of an interval treatment in a patient affected with Wiscott-Aldrich syndrome with transfer factor between the 6th and 14th month of life had good clinical success initially which coincided with the normalization of in vitro stimulation of the patient's lymphocytes. Only short-term (in vitro) measurable effects could be achieved by the transfer factor. Whereas clinical therapy effects were diminishing from treatment phase to treatment phase, it was possible to observe further positive results in paraclinical findings. It was only MLC reactivity that correlated with the clinical picture. Etiologically, all findings gained speak in favour of a helper cell defect and/or monocyte defect. TF therapy was not repeated because of the findings obtained and the clinical course.

Publication Types:
• Case Reports

PMID: 6198251 [PubMed - indexed for MEDLINE]
Orv Hetil. 1979 Sep 30;120(39):2361-6. Related Articles, Links

[Successful treatment of Wiscott-Aldrich syndrome with transfer factor]

[Article in Hungarian]

Endre L, Nekam K, Osvath P, Nagy M, Karoly U, Uhl K.

Publication Types:
• Case Reports
• Clinical Trial

Clin Exp Immunol. 1975 Sep;21(3):520-4. Related Articles, Links

Randomized trial of transfer factor treatment of human warts.

Stevens DA, Ferrington RA, Merigan TC, Marinkovich VA.

Dialysed transfer factor, prepared from the leucocytes of a donor whose warts had undergone recent spontaneous regression, was used in the treatment of a child with the Wiskott--Aldrich syndrome. The child then had a spontaneous regression at multiple warty areas. A similar relationship was seen in four otherwise healthy patients in a pilot study. A randomized double-blind study of thirty patients failed to confirm a causal relationship between the transfer factor therapy (equivalent to 2-1 X 10(8) leucocytes) and wart regressions. The need for randomized trials of transfer factor therapy for diseases with a variable natural history is emphasized.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 1106927 [PubMed - indexed for MEDLINE]
Clin Immunol Immunopathol. 1979 Aug;13(4):407-12. Related Articles, Links

Effects of therapy with dialyzable leukocyte extracts containing transfer factor activity on antibody-dependent cytotoxic activity in humans.

Nekam K, Lang I, Torok K, Kalmar L, Gergely P, Petranyi G.

PMID: 226302 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1980 Mar-Apr;8(2):125-9. Related Articles, Links

Transfer factor: specific and nonspecific effects and chemical characteristics of dialyzable leukocyte lysates (DLL). Part II. Reconstituting effects dialyzable leukocyte lysates. (Second of three parts).

Schindler TE, Baram P.

PMID: 7457287 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1980 May-Jun;8(3):203-12. Related Articles, Links

Transfer factor: specific and nonspecific effects and chemical characteristics of dialyzable leukocyte lysates (DLL). Part III. Biochemical characterization. (third of three parts).

Ablin RJ.

PMID: 7405767 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1980 Jan-Feb;8(1):53-60. Related Articles, Links

Transfer factor: specific and nonspecific effects and chemical characteristics of dialyzable leukocyte lysates (DLL). Part I. Introduction. (first of three parts).

Ablin RJ.

PMID: 6996464 [PubMed - indexed for MEDLINE]
Cell Immunol. 1976 Dec;27(2):323-7. Related Articles, Links

Serial transfer of delayed hypersensitivity with dialyzable transfer factor.

Kirkpatrick CH, Smith TK.

PMID: 795550 [PubMed - indexed for MEDLINE]
1: Adv Exp Med Biol. 1973;29(0):343-50.
Related Articles, Links

Immunological and clinical effects of transfer factor in anergic subjects.

Kirkpatrick CH, Rich RR, Smith TK.

PMID: 4604570 [PubMed - indexed for MEDLINE]

Scand J Immunol. 1974;3(2):223-8. Related Articles, Links

The principle of immunopotentiation in treatment of rheumatoid arthritis: effect of transfer factor.

Froland SS, Natvig JB, Hoyeraal HM, Kass E.

PMID: 4207152 [PubMed - indexed for MEDLINE]
Scand J Rheumatol. 1974;3(3):113-7. Related Articles, Links

A new principle of immunotherapy in rheumatoid arthritis: treatment with transfer factor.

Kass E, Froland SS, Natvig JB, Blichfeldt P, Hoyeraal HM, Munthe E.

PMID: 4428189 [PubMed - indexed for MEDLINE]

Cell Immunol. 1973 Jul;8(1):120-35. Related Articles, Links

Immunologic and clinical improvement of progressive coccidioidomycosis following administration of transfer factor.

Graybill JR, Silva J Jr, Alford RH, Thor DE.
Cell Immunol. 1974 Mar 15;10(3):371-9. Related Articles, Links

Transfer factor therapy in a case of complex immunodeficiency.

Arala-Chaves MP, Proenca R, De Sousa M.

Oct 29 2004 13:56:18
Cell Immunol. 1974 Apr;12(1):160-3. Related Articles, Links

Short communications. Evidence for prompt and intense reconstitution of cell-mediated immunity by means of transfer factor in a case of complex immune deficiency.

Arala-Chaves M, Ramos MT, Rosado RM.

PMID: 4458960 [PubMed - indexed for MEDLINE]
J Pediatr. 1975 May;86(5):818-9. Related Articles, Links

Letter: Combined immunodeficiency and transfer factor.

Strauss RG, Hake DA.

Publication Types:
• Case Reports

Ann Allergy. 1976 Oct;37(4):267-74. Related Articles, Links

Asthma and T cell immunodeficiency: improvement with transfer factor and immunopeptide.

Khan A, Sellars WA, Pflanzer J, Hill JM, Thometz D, Haenke J.

Publication Types:
• Case Reports

PMID: 1086620 [PubMed - indexed for MEDLINE]
Lancet. 1975 Oct 11;2(7937):702. Related Articles, Links

Letter: Transfer factor in severe atopic disease.

Strannegard IL, Hanson LA, Lindholm L, Mobacken H, Strannegard O.

Publication Types:
• Case Reports

PMID: 52068 [PubMed - indexed for MEDLINE]
Cell Immunol. 1975 Oct;19(2):219-29. Related Articles, Links

Report of a patient with T-cell deficiency and normal B-cell function: a new immunodeficiency disease with response to transfer factor.

Ballow M, Good RA.

Publication Types:
• Case Reports
Am J Med. 1980 Jun;68(6):955-61. Related Articles, Links

Chorioretinitis with a combined defect in T and B lymphocytes and granulocytes. A new syndrome successfully treated with dialyzable leukocyte extracts (transfer factor).

Kyong CU, Wilson GB, Fudenberg HH, Goust JM, Richardson P, Echerd J.

A patient with immune deficiency, recurrent pyogenic infections and active chorioretinitis is described; in addition to agammaglobulinemia, both quantitative and qualitative T-cell deficiencies were documented. Furthermore, the patient's

granulocytes (polymorphonuclear leukocytes), although normal in their bactericidal capacity for Staphylococcus, responded poorly to both leukocyte migration inhibition factor and neutrophil immobilizing factor obtained from normal cells. The immunologic features of this patient appear to comprise a new syndrome. Remarkable diminution of the ocular lesions and increased visual acuity occurred within two months after the initiation of therapy with dialyzable leukocyte extracts (transfer factor). Concurrent testing of the patient's cell-mediated immunity showed increased numbers of circulating T lymphocytes and improved T-cell function following dialyzable leukocyte extract [DLE] therapy. The dramatic clinical results indicate that similar therapy may prove to be beneficial in other patients with chorioretinitis and T-cell deficiency.

Publication Types:
• Case Reports

PMID: 6992573 [PubMed - indexed for MEDLINE]
Clin Lab Immunol. 1984 Feb;13(2):51-8. Related Articles, Links

Guidelines for immunotherapy of antigen-specific defects with transfer factor.

Wilson GB, Fudenberg HH, Keller RH.

Dialyzable leukocyte extracts (DLE) containing transfer factor (TF) with documented specificity for one or more microbial antigens have shown previously variable clinical effectiveness in treating many infectious diseases caused by viruses, fungi, protozoa and mycobacteria. The efficacy has sometimes been strong, and at other times dubious, in treating patients with inherited or presumably "acquired" immunodeficiency diseases refractory to standard therapy. The recent development of assays for screening leukocyte donors of DLE, for monitoring recipients, and especially for determining the potency of various DLE preparations containing antigen-specific TF and for predicting the clinical course of disease have, in our hands, greatly improved the likelihood of successful immunotherapy with TF. Two representative cases are reported, one involving a patient with an antigen selective defect to Candida, and another involving a patient with an antigen selective defect to Mycobacterium fortuitum. Both patients responded as judged by laboratory tests and clinical improvement when treated with certain DLE preparations but not with others. Finally, certain DLE preparations appeared to suppress cell-mediated immunity in vivo and this suppression could be predicted by in vitro tests. Based on these results, guidelines for optimal therapy with DLE are proffered .

Publication Types:
• Case Reports

PMID: 6202873 [PubMed - indexed for MEDLINE]
J Immunol. 1981 Jan;126(1):80-2. Related Articles, Links

Antigen-specific activity of murine leukocyte dialysates containing transfer factor on human leukocytes in the leukocyte migration inhibition (LMI) assay.

Borkowsky W, Suleski P, Bhardwaj N, Lawrence HS.

We report on the extension of the direct leukocyte migration inhibition (LMI) test as an assay for antigen-specific activity in human leukocyte dialysates (DLE) containing transfer factor to an evaluation of antigen-specific activity in DLE prepared from inbred mice. Murine DLE was observed to cause antigen-dependent and antigen-specific effects on the inhibition of migration of nonimmune human leukocyte populations. Pulsing of nonimmune human leukocyte with DLE preparations from BALB/c and SJL mice immunized with Candida, diphtheria toxoid, and SK-SD resulted in their inhibition of migration in the presence of the respective antigens. The antigen-specific activity in murine DLE was found to be present in lymph node cell preparations and to be absent from spleen cell preparations of the same donors. The activity of DLE in lymph node cells was found to be present in the theta-cell enriched subpopulation of nonadherent lymphocytes after passage through nylon wool columns. The antigen-specific activity of murine DLE, as we have reported for human DLE, was found to reside in the < 3500 dalton dialysis fraction and not in the < 3500 dalton fraction. We conclude that nonimmune human leukocytes in the LMI test provide a suitable assay for the detection of antigen-specific activity in murine DLE as well as that in human DLE. Additionally, murine DLE is active across species barriers and appears to share properties with human DLE.

PMID: 6161170 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):1-5. Related Articles, Links

Transfer factor--current status and future prospects.

Lawrence HS, Borkowsky W.

Department of Medicine, New York University Medical Center, New York, NY 10016, USA.

We have detected new clues to the composition and function of "Transfer Factor" using the direct Leucocyte Migration Inhibition (LMI) test as an in vitro assay of Dialysates of Leucocyte Extracts (DLE). This approach has revealed two opposing antigen-specific activities to be present in the same > 3500 < 12,000 DA dialysis fraction - one activity is possessed of Inducer/Helper function (Inducer Factor). The opposing activity is possessed of Suppressor function (Suppressor Factor). When non-immune leucocyte populations are cultured with Inducer Factor they acquire the capacity to respond to specific antigen and inhibition of migration occurs. This conversion to reactivity is antigen-specific and dose-dependent. When immune leucocyte populations are cultured with Suppressor Factor their response to specific antigen is blocked and Inhibition of Migration is prevented.

Publication Types:
• Review
• Review, Tutorial

PMID: 8993750 [PubMed - indexed for MEDLINE]
J Lab Clin Med. 1979 May;93(5):800-18. Related Articles, Links

Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. 1. Antigen-dependent inhibition and antigen-independent inhibition and enhancement of migration.

Wilson GB, Fudenberg HH, Horsmanheimo M.

The effects of DLE containing TFd activity from immune human donors on PBL, obtained from individuals nonresponsive to either PPD or Cocci antigen, were evaluated in vitro by the agarose LMI technique. Several different preparations of DLE were employed to evaluate the specificity and reproducibility of the effects: (1) from donors skin test positive to PPD but negative to Cocci, (2) from donors skin test negative to PPD but positive to Cocci, (3) from donors skin test positive to both antigens, and (4) from donors skin test negative to both antigens. With PBL from other human donors used as target cells in the direct agarose LMi technique, three types of effects were demonstrated for all preparations of DLE: (1) antigen-dependent specific LMI, (2) antigen-independent or nonspecific LMI, and (3) antigen-independent enhancement of migration. The demonstration of each activity was found to depend on the concentration of DLE used and the time allowed for migration. In experiments employing purified PMN and MNL as target cells and a two-step indirect LMI assay, it was shown that the antigen-independent effects resulted from the direct of components in DLE on PMN. The antigen-independent inhibition was shown not to result from toxic effects of DLE. It was produced by DLE but not by dialyzable liver or skin extracts when tested using an amount equivalent to DLE as judged by the absorbance at 260 and 280 nm. The antigen-dependent LMI was found to require secretion of a soluble mediator of molecular weight near 69,000, believed to be LMI. Our results indicate that the agarose LMI technique is a useful in vitro assay for studies of the mechanism of action of components in DLE which can specifically convert nonimmune lymphocytes to a measurable antigen-sensitive state (i.e., transfer factor). The antigen-independent effects of DLE may be responsible in part for previously reported nonspecific beneficial effects of DLE when used in immunotherapy.

PMID: 429876 [PubMed - indexed for MEDLINE]
Lab Clin Med. 1979 May;93(5):819-37. Related Articles, Links

Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. II. Separation and partial characterization of the components in DLE producing antigen-dependent and antigen-independent effects.

Wilson GB, Fudenberg HH.

Previous studies have shown that DLEs with TFd activity produce both Ag-dependent specific effects (mediated by TFd) and Ag-independent effects on CMI as demonstrated in vitro by agarose LMI. In the present study, Sephadex G-25 gel filtration provided a simple method for separating the DLE components responsible for each effect into distinct fractions. Ag-independent LMI was produced predominantly by Sephadex fraction I, of MW greater than 5000. The active components, further purified on Bio-Gel P-10, were shown to be of MW 14,000 to 17,000 and to contain both polypeptide and ribonucliotide material. The Ag-independent LMI activity was stable to heating at 56 degrees C for 30 min but was partially destroyed at 80 degrees C for 30 min, and the responsible components were shown to act on PMN directly. Ag-independent ELM was produced exclusively by material in Sephadex G-25 fraction V and also acted directly on PMN, whereas the Ag-dependent specific LMI activity was found predominantly in fraction IVb and to a lesser extent in fraction V and could not be detected in a direct assay using only PMN. In addition, a new activity, designated "Ag-dependent ELM activity," which caused increased migration in the presence of Ag, was found in Sephadex fraction IVa. This latter activity might mask the Ag-dependent LMI activity in fraciton IVb. Bio-Gel P-2 chromatography separated the components producing Ag-dependent and Ag-independent effects in fraction V into two separate subfractions (Va and Vb) of MW 1100 to 2000 and less than 900. The activity in fraction IVb eluted at a position identical to that of the components in fraction Va on Bio-Gel P-2. Fractions Va and Vb contained both polypeptide and ribonucleotide material. The Ag-dependent specific

LMI or TFd activity was found to be partially inactivated at 56 degrees C and completely destroyed at 80 degrees C. The components responsible for this TFd activity were further purified by HPLC on ODS resin. The TFd activity was mediated by components with retention times much greater than that of adenosine 3'-monophosphate. The active fraction was composed of both polypeptide and ribonucleotide material but did not contain deoxyribonucleotides.

PMID: 429877 [PubMed - indexed for MEDLINE]
Allergy Clin Immunol. 1979 Jul;64(1):56-66. Related Articles, Links

Effects of dialyzable leukocyte extracts (DLEs) with transfer factor activity on leukocyte migration in vitro. III. Characterization of the antigen-independent migration inhibition factor in DLEs as a neutrophil immobilizing factor.

Wilson GB, Smith CL, Fudenberg HH.

In earlier evaluations of the agarose LMI assay as an in vitro test for studying the nature and mechanism of action of TF, we reported the existence of a component in human DLEs which caused noncytotoxic inhibition of the random migration of human PMNs. The LMI was not dependent on the stimulation of viable mononuclear leukocytes by antigen or mitogen to effect the release of mediators of cellular immunity such as LIF; rather, the LMI was promoted by the direct action of a preexisting component in DLEs on PMNs. We now present evidence that this "antigen-independent" LMI activity in DLE'S is similar to a NIF shown previously by Goetzl and co-workers to be present in acid extracts of leukocytes and to be released by phagocytosing PMNs. The comparison is drawn from several parameters: (1) cellular origin, (2) molecular weight, (3) target cell, (4) susceptibility to inactivation by heating or by incubation with pronase, trypsin, or chymotrypsin, and (5) ability to cause noncytotoxic inhibition of random migration or chemotaxis of PMNs.

PMID: 447952 [PubMed - indexed for MEDLINE]
Clin Immunol Immunopathol. 1980 May;16(1):90-102. Related Articles, Links

Effects of dialyzable leukocyte extracts (DLE) with transfer factor activity on leukocyte migration in vitro. IV. Two distinct effects of DLE on leukocyte migration can be produced by prostaglandins.

Wilson GB, Fudenberg HH, Jonsson HT Jr, Smith CL.

PMID: 7379353 [PubMed - indexed for MEDLINE]
Trans Assoc Am Physicians. 1978;91:295-332. Related Articles, Links

Distinct components in dialyzable leukocyte extracts (DLE) have specific and nonspecific effects on cellular immunity as shown by leukocyte migration inhibition.

Wilson GB, Fudenberg HH, Bahm VJ.

PMID: 754397 [PubMed - indexed for MEDLINE]
1: Hokkaido Igaku Zasshi. 1985 Sep;60(5):763-8.
Related Articles, Links

[Studies of an assay system for dialyzable leukocyte extracts (DLE)--influence of DLE on leukocyte migration inhibition test by HBsAg]

[Article in Japanese]

Hashimoto Y, Sekiguchi S.

In order to examine the suitability of leukocyte migration inhibition test (LMIT) in the capacity of in vitro assay system for dialyzable leukocyte extracts (DLE), the effect of DLE on hepatitis B and its antigen-specificity, the migration inhibitory activities to purified hepatitis B surface antigen (HBsAg) was measured using the leukocyte MIF test with DLEs obtained from HBsAb-positive or HBsAb-negative blood. The direct LMIT using agarose plate was modified according to the technique of Clausen et al. In spite of our assay system was dose-dependent for PPD, a significant response for purified HBsAg was not observed. However, some meaningful migration inhibition appeared when HBsAg and DLE were added simultaneously to the migration cells. From these results, it is concluded that DLE has antigen-specific and/or antigen non specific influences to the cell-mediated immunity for HBsAg Though some problems remain, we think our results are interesting, since the assay system for DLE has not been established and our study is closely related to the effect of DLE concerning hepatitis B.

PMID: 3908264 [PubMed - indexed for MEDLINE]
J Immunol. 1981 Jan;126(1):80-2. Related Articles, Links

Antigen-specific activity of murine leukocyte dialysates containing transfer factor on human leukocytes in the leukocyte migration inhibition (LMI) assay.

Borkowsky W, Suleski P, Bhardwaj N, Lawrence HS.

We report on the extension of the direct leukocyte migration inhibition (LMI) test as an assay for antigen-specific activity in human leukocyte dialysates (DLE) containing transfer factor to an evaluation of antigen-specific activity in DLE prepared from inbred mice. Murine DLE was observed to cause antigen-dependent and antigen-specific effects on the inhibition of migration of nonimmune human leukocyte populations. Pulsing of nonimmune human leukocyte with DLE preparations from BALB/c and SJL mice immunized with Candida, diphtheria toxoid, and SK-SD resulted in their inhibition of migration in the presence of the respective antigens. The antigen-specific activity in murine DLE was found to be present in lymph node cell preparations and to be absent from spleen cell preparations of the same donors. The activity of DLE in lymph node cells was found to be present in the theta-cell enriched subpopulation of nonadherent lymphocytes after passage through nylon wool columns. The antigen-specific activity of murine DLE, as we have reported for human DLE, was found to reside in the < 3500 dalton dialysis fraction and not in the < 3500 dalton fraction. We conclude that nonimmune human leukocytes in the LMI test provide a suitable assay for the detection of antigen-specific activity in murine DLE as well as that in human DLE. Additionally, murine DLE is active across species barriers and appears to share properties with human DLE.
Cell Immunol. 1985 Feb;90(2):295-302. Related Articles, Links

Transfer of osteosarcoma-specific cell-mediated immunity in hamsters by rabbit dialyzable leukocyte extracts.

Tsang KY, Fudenberg HH, Pan JF.

We have investigated the transfer of specific cell-mediated immunity (CMI) to osteosarcoma-associated antigens (OSAA) to hamsters with dialyzable leukocyte extracts (DLE) from OSAA-immunized rabbits. The transfer of specific CMI was determined by leukocyte adherence inhibition (LAI) assay and skin testing. DLE was prepared from rabbits immunized with OSAA, purified protein derivative (PPD), or fibrosarcoma cell plasma membrane preparation (FSM). Control DLE was prepared from rabbits injected with 0.85% NaCl. Significant leukocyte adherence inhibition was observed with leukocytes from hamsters that had received OSAA-specific, PPD-specific, and FSM-specific rabbit DLE, when OSAA, PPD, and FSM were used as antigens, respectively. Similarly, significant ear swelling after injection of OSAA, PPD, or FSM was observed only in hamsters that had received DLE from rabbits immunized with OSAA, PPD, or FSM, respectively. These results suggest that CMI specific for OSAA, PPD, or FSM can be transferred to normal hamsters by DLE from immunized rabbits.

PMID: 3855389 [PubMed - indexed for MEDLINE]
Int Arch Allergy Appl Immunol. 1984;73(2):146-50. Related Articles, Links

Counter inhibitor: a low molecular weight cytokine derived from human leukocyte dialysates reverses antigen dependent PMN and macrophage migration inhibition.

Farmer JL, Rosenberg JS, Hester RB, Gottlieb AA.

A low molecular weight component, termed counter inhibitor (CI), has been partially purified from human dialyzable leukocyte extracts. Addition of CI to either a direct leukocyte or macrophage migration inhibition system results in reversal of antigen-induced migration inhibition. CI activity requires the presence of antigen for expression, but does not require that the donor of the CI be immune to the antigen used in the migration inhibition assay. Reversal of migration inhibition by CI appears to be a consequence of its ability to prevent PMNs or macrophages from responding to lymphokines which induce migration inhibition.
Rev Alerg. 1992 Nov-Dec;39(6):126-32. Related Articles, Links

[In vitro transfer of immunity against PPD with dialyzable extract of leukocytes from human colostrum]

[Article in Spanish]

Martinez-Cairo Cueto S, Alasio-Chavez C, Davila Velazquez JR.

Departamento de inmunologia, Hospital de Pediatria, Mexico, DF.

The aim of this study is to demonstrate the transference of PPD hypersensibility in an in vitro model, with dialysable colostral leukocyte extract (DCLE) of PPD+ and PPD-mothers, through measurements of leukocyte migration inhibition factor activity (LIF) from blood obtained of the umbilical cord of newborns from PPD+ mothers. The results show that DCLE PPD+ incubated with leukocytes of newborns from PPD- mothers had inhibition of leukocyte migration compared with migration of leukocytes incubated with DCLE PPD-. These results suggest that in this in vitro model, DCLE transfers hypersensibility to PPD.

PMID: 1492196 [PubMed - indexed for MEDLINE]
Vet Immunol Immunopathol. 1992 Apr;32(1-2):103-21. Related Articles, Links

Stabilization of Salmonella-specific dialyzable leukocyte extracts.

Mikula I, Pistl J, Rosocha J.

Department of Microbiology, Immunology and Animal Hygiene, University of Veterinary Medicine, Kosice, Czechoslovakia.

Activity of Salmonella-specific dialyzable leukocyte extracts (DLE) prepared from mesenteric lymphatic nodes of calves and stabilized with bovine albumin was studied in this work. The effect of ambient temperature and storage period on the activity of DLE was evaluated. Testing for DLE activity by means of capillary leukocyte migration inhibition (LMI) assay showed that DLE stabilized with albumin retained 60% of its activity for 12 months of storage at 4 degrees C. This level of activity was retained in the native DLE (without albumin) kept at -20 degrees C. DLE stabilized with albumin and stored for 12 months at 4 degrees C inhibited the penetration of salmonellae into the liver and spleen, and their colonization in the gastrointestinal tract was significantly reduced.

PMID: 1604793 [PubMed - indexed for MEDLINE]
Thymus. 1981 Feb;2(4-5):257-6. Related Articles, Links

Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. V. Antigen-specific lymphocyte responsiveness can be initiated by two structurally distinct polyribonucleopeptides.

Wilson GB, Paddock GV, Fudenberg HH.

Human transfer factors (TF) active in specifically inducing responsiveness in human thymus-derived (T) lymphocytes previously nonresponsive to purified protein derivative from Myobacterium tuberculosis (PPD) or to Coccidioides immites (Cocci) in vitro were isolated from the dialyzable portion of extracts of immune leukocytes (DLE). Each TF segregated into two active fractions after high-pressure reverse-phase liquid chromatography (HPLC), suggesting the presence of two TF components in DLE for each antigen specificity. Determination of the structures of both TF components specific for PPD was accomplished by evaluating their activity after incubation with various endonucleases, exonucleases, phosphatases, peptidases and a protease. The results indicated that both PPD-specific TF components are oligoribonucleopeptides but that they are structurally distinct. Simplest-case molecular models were constructed on the basis of the data obtained.

PMID: 6165106 [PubMed - indexed for MEDLINE]
Thymus. 1982;4(6):335-50. Related Articles, Links

Bovine 'transfer factor': an oligoribonucleopeptide which initiates antigen-specific lymphocytes responsiveness.

Wilson GB, Paddock GV, Fudenberg HH.

Bovine transfer factor (TF)--active in initiating specific responsiveness in human thymus-derived (T) lymphocytes to purified protein derivative from Mycobacterium tuberculosis (PPD) in vitro--was partially purified from the dialyzable portion of medium from immune lymph node cells (DLNE). Its physiochemical properties and structure were determined by methods previously employed to characterize human PPD-specific TF isolated from dialyzable leukocyte extracts (DLE). Bovine TF had a molecular weight (MW) of 1100-3000, was destroyed by heating at 56 or 80 degrees C for 30 min, was soluble in water but not in phenol or ether, and could be precipitated with ethanol. Bovine TF activity eluted as a single peak after high-pressure reverse-phase liquid chromatography (HPLC); the active moiety contained at least one free co-planar cis-diol group, as shown by boronate affinity chromatography. Additional structural features were deduced by evaluating TF activity after incubation with various endonucleases, exonucleases, and peptidases, a phosphatase, and a protease. The combined results indicate that bovine TF specific for PPD is an oligoribonucleopeptide. A simplest case molecular model was constructed on the basis of the data obtained. A comparative evaluation of the physicochemical properties and structural features of bovine TF and human TF specific for PPD indicated striking similarities and some differences.

PMID: 6191411 [PubMed - indexed for MEDLINE]

Immunol. 1979 Mar;122(3):1091-8. Related Articles, Links

Human transfer factors: structural properties suggested by HPRP chromatography and enzymatic sensitivities.

Burger DR, Vandenbark AA, Dunnick W, Kraybill W, Daves GD, Vetto RM.

Leukocyte extracts containing human transfer factor (TF) were fractionated by exclusion chromatography, and the active fraction (Sephadex G25, Fraction IIIa) was subjected to high pressure, reverse phase (HPRP) chromatography and enzymatic degradation. TF activity was assessed by the systemic transfer of dermal skin test reactivity from KLH-immunized donors to naive recipients. Preparative HPRP chromatography resolved Fraction IIIa into multiple chromophoric regions, two of which demonstrated transfer of KLH reactivity. Alkaline phosphatase treatment of Fraction IIIa converted the major ultraviolet-absorbing component, 5'-inosine monophosphate, to inosine and resulted in TF activity being restricted to one region. This HPRP region (R1A) contained less than 1% of the UV254 active material in Fraction IIIa but greater than 90% of the reactivity. The sensitivity of TF to pronase, proteinase K, phosphodiesterase I, and phosphodiesterase II was evaluated by inhibition of systemic transfer of KLH reactivity. Pronase and proteinase K destroyed systemic transfer activity and the pronase destruction could be inhibited with traysylol. Phosphodiesterase I, a 3' exonuclease, destroyed activity, whereas phosphodiesterase II, a 5' exonuclease, did not. The data are consistent with a phosphodiester-containing polypeptide in the structure of human TF for KLH reactivity.

PMID: 448071 [PubMed - indexed for MEDLINE]
Oncology. 1975;32(5-6):269-74. Related Articles, Links

Transfer factor - hypotheses for its structure and function.

Shifrine M, Scibienski R.

Transfer factor (TF) is a dialyzable extract from primed lymphocytes that is able to transfer specific delayed hypersensitivity from one animal to another. On the basis of available data we suggest that TF is a polypeptide with a molecular weight below 15,000 daltons. We hypothesize that TF is the variable light or heavy chain domain of immunoglobulin: such a molecule conforms with the accepted properties of TF and also has the necessary specificity requirements. We also hypothesize that TF is part of a receptor site. beta-2-microglobulin, a molecule that is an integral part of cell surfaces, could be the anchor for TF. beta-2-microglobulin has homologies with the constant portion of immunoglobulin light or heavy chain and thus would combine with the variable domain (TF) to form a complete receptor site for a specific antigen. The properties of TF suggest its mode of action, which is discussed in detail in the text. The biologic advantages of TF is its ability to confer immediate (immunologie specific) protection while the 'normal' immune response develops.

PMID: 778717 [PubMed - indexed for MEDLINE]
Acta Virol. 1992 May;36(3):231-8. Related Articles, Links

Isolation and purification of HSV-1 specific transfer factor produced by HSV-1 immunized goat leukocyte dialysate.

Qi HY, Wan ZF, Su CZ.

Department of Biochemistry, Fourth Military Medical University, Xian, P.R. China.

A herpes simplex virus type 1 (HSV-1)-specific transfer factor (TF), was separated and purified from the leukocyte dialysate of goats immunized with HSV-1 using affinity chromatography on antigen-sorbent and reversed phase high performance liquid chromatography (RP-HPLC). The antigen-specific activities of the starting dialysate and the isolated TF component (s) were examined by 51Cr-labelled leukocyte adherence inhibition (51Cr LAI) assay. The analytical hydrophobic interaction HPLC (HI-HPLC) and isoelectric focusing (IEF) techniques were employed to evaluate the purity and the isoelectric point (PI) of isolated TF component(s). The experiments provided a two-step procedure for purifying the TF material from the starting dialysate. It seems that the purified active TF component (PTFC) was specific for HSV-1. The specific PTFC activity was increased 10,000-fold as compared with the activity of the dialysate. The active moiety appeared as a single band in the IEF gel as demonstrated by silver staining; it was hydrophilic and its PI was pH 4.48.

PMID: 1360750 [PubMed - indexed for MEDLINE]
Acta Virol. 1988 Jan;32(1):6-18. Related Articles, Links

De novo initiation of specific cell-mediated immune responsiveness in chickens by transfer factor (specific immunity inducer) obtained from bovine colostrum and milk.

Wilson GB, Poindexter C, Fort JD, Ludden KD.

Amtron, Inc., Charleston, South Carolina.

Transfer factors (TF) were prepared from colostrum and milk of bovines previously immunized with antigens obtained from Coccidioides immitis, infectious bovine rhinotracheitis virus, or from the viral agents responsible for avian Newcastle disease, laryngotracheitis disease or infectious bursal disease. The ability of bovine TF to transfer specific cell-mediated immune responsiveness to a markedly xenogenic species was studied using specific pathogen free (SPF) and standard commercial (SC) chickens as model recipients. Cell-mediated immune responsiveness was documented using one or more of the following for each antigen (organism) studied: (a) an in vitro chicken leukocyte (heterophil) migration inhibition assay; (b) delayed-wattle reactivity; or (c) protection from clinical disease. Chicken TFs obtained from spleens of immune donors were evaluated in parallel to bovine TF's in selected comparative studies. Bovine TF also referred to as specific immunity inducer (SII), and chicken TF were found to initiate antigen-specific cell-mediated immunity de novo in previously non-immune SPF chickens as well as in SC chickens despite the presence of maternally acquired humoral antibody which may serve as a "barrier" to immunization of SC chickens when commercially available vaccines are administered by parenteral routes. Bovine TF's specific for laryngotracheitis virus or infectious bursal disease virus afforded protection equal to that found for commercially available vaccines. Bovine TF's action was rapid (less than a day) and of relatively long duration at least 35 days.

PMID: 2897772 [PubMed - indexed for MEDLINE]
Immunology. 1978 Aug;35(2):247-56. Related Articles, Links

An investigation into the antigen-specificity of transfer factor in its stimulatory action on lymphocyte transformation.

Salaman MR.

Dialysable transfer factor (TF) was prepared from the buffy-coat cells of donors with known cell-mediated reactivity to tuberculin (PPD), streptococcal protein (SKSD) and diphtheria toxoid (DT). The effect of such preparations on the transformation by these antigens of lymphocytes from tuberculin-negative donors was investigated. Transformation was determined as incorporation of tritiated thymidine. The concentrations of SKSD and DT were adjusted for different lymphocyte donors so as to give, in the absence of TF, a low index of transformation (less than 10-fold) comparable to that obtained with PPD. TF from tuberculin-positive donors stimulated antigen-induced transformation by on average approximately 2-fold whereas TF from tuberculin-negative donors generally had little effect. This was so not for PPD as antigen but also for SKSD and DT, and sensitivity of TF donor to SKSD of DT was not a determining factor. TF also frequently increased background transformation in the absence of antigen. Although a small effect, this ability tended to reflect the activity of TF in the presence of antigen. It is concluded that neither the whole nor any significant part of this enhancement of transformation can be ascribed to an antigen-specific factor. Tuberculin-positive donors apparently yield a higher level of non-specific factor and possible reasons for this are discussed. The factor active in transformation may be responsbile for the TF phenomenon in vivo.

PMID: 86502 [PubMed - indexed for MEDLINE]
Cell Immunol. 1977 Jan;28(1):158-66. Related Articles, Links

Augmentation of 3H-thymidine incorporation by human lymphocytes in the presence of antigen and fractions of dialyzable transfer factor: a nonspecific phenomenon.

Littman BH, Hirschman EM, David JR.

PMID: 64313 [PubMed - indexed for MEDLINE]
Panminerva Med. 1993 Sep;35(3):149-53. Related Articles, Links

Transfer in vivo of tuberculin hypersensitivity by sensitised lymphocytes.

Fazio M, Calabrese F, Giacomasso S, Meina G, Negri L, Mastromatteo V.

Chair of Medical Oncology, University of Turin, Italy.

An account is given of the experimental in vivo transfer of PPD-specific delayed hypersensitivity with a very small number of autologous lymphocytes pre-sensitised with PPD-specific transfer factor (TF). Transfer was assessed in 17 volunteers both in vivo by means of the Mantoux skin reaction, and in vitro by means of the leukocyte migration inhibition test, the lymphocyte locomotion test, and the leukocyte adherence inhibition test. Positivization of the tests suggests that TF triggers a reaction which expands the effect of hypersensitivity.

PMID: 8090529 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1979 Jul;37(1):50-7. Related Articles, Links

Human transfer factor in vitro. II. Augmentation of the secretion of leucocyte migration inhibitory factor (LIF) by leucocyte dialysate and by its components L-serine and glycine.

Ashorn RG, Rasanen L, Marnela KM, Krohn KJ.

The effect of human transfer factor (TF) or its components L-serine and/or glycine in tuberculin (PPD), or leucoagglutinin (LA) induced leucocyte migration inhibitory factor (LIF) secretion was studied. Augmentation of LIF secretion was seen with low concentration (= 0.078 g/l) of TF when lymphocytes were cultured in minimum essential medium for suspension cultures (MEM-S), a culture medium lacking L-serine and glycine. High concentrations (0.3125-5.0 g/l dry weight) of TF were inhibitory in MEM-S. In RPMI 1640, a culture medium containing L-serine and glycine, TF was either inhibitory or had no effect. The combination of L-serine and glycine, at concentrations equivalent or lower than the optimum of TF, had an augmenting effect on LIF secretion identical to that of TF, but no inhibition at higher concentrations was seen. The results indicate that human TF contains components which have suppressive or augmenting effects on LIF secretion in vitro. The augmenting effect may be mainly due to L-serine and glycine and thus not related to TF's activity in vivo.

PMID: 385187 [PubMed - indexed for MEDLINE]
J Immunol. 1977 Jun;118(6):1944-50. Related Articles, Links

Specificity and structural analysis of a guinea pig transfer factor-like activity.

Dunnick WA, Bach FH.

A transfer factor-like activity was prepared by Sephadex G-25 chromatography of immune guinea pig leukocyte lysates. This isolated material leads to antigen-dependent migration inhibition and thymidine uptake by nonimmune lymphoid cells. Tests of the "transfer factor" from guinea pigs immunized to either ovalbumin or bovine gamma-globulin demonstrated the donor specificity of the in vitro activity. The activity is susceptible to heat (56 degrees C), alkali (0.5 M sodium hydroxide), pronase, and phosphodiesterase. The pronase susceptibility is blocked by traysylol, a protease inhibitor; the phosphodiesterase susceptibility is not bocked by traysylol. The guinea pig factor was purified further by alkaline phosphatase treatment. Sephadex G-25 chromatography, and DEAE-cellulose chromatography. The final product, active in vitro, represents about 0.03% of the cellular material absorbing 260 nm light, and contains polymerized amines and phosphate. Gel electrophoresis of the fluram-reactive components suggests a limited heterogeneity of the DEAE-cellulose-purified material. These data are consistent with the active "transfer factor" molecule including both peptide and phosphate-containing components.

PMID: 68075 [PubMed - indexed for MEDLINE]
Panminerva Med. 1993 Jun;35(2):96-100. Related Articles, Links

Transfer in vitro of tubercolin hypersensitivity by sensitised lymphocytes.

Fazio M, Calabrese F, Giacomasso S, Negri L, Mastromatteo V.

Chair of Medical Oncology, University of Turin, Italy.

An account is given of the experimental in vitro transfer of PPD-specific delayed hypersensitivity to peripheral leukocytes pulsed with a very small portion of autologous lymphocytes pre-sensitised with PPD-specific transfer factor (TF). Transfer was assessed by means of the leukocyte migration inhibition test, the lymphocyte locomotion test, and the leukocyte adherence inhibition test. These tests were positivized in all the experiments. It is suggested that these results indicate that TF does not act in itself, but triggers a reaction that expands the effect of hypersensitivity.

PMID: 8414630 [PubMed - indexed for MEDLINE]
Tohoku J Exp Med. 1980 Jul;131(3):271-83. Related Articles, Links

Transfer factor from BCG-sensitized mice.

Sasaki K, Suzuki F, Ishida N.

A mouse model was established for the study of transfer factor (TF). TF was extracted from the spleens of sensitized

mice and examined for activity by the footpad test, which showed that mouse and human TF possessed similar properties. Parenteral administration of TF imparted to unsensitized mice immunologically specific, delayed type hypersensitivity within 24 hr. The magnitude of the response the recipients was proportional to the dose of TF. TF activity was relatively heat-stable, detectable in a fraction of molecular weight of ca 1,000 and apparently contained nucleic acids. Nude mice responded negatively to TF but following administration of viable naive spleen cells a positive response was observed, which suggests that the thymus plays an important role in the expression of TF phenomenon and that the target of TF is the T cells.

PMID: 6158138 [PubMed - indexed for MEDLINE]

Mol Immunol. 1992 Feb;29(2):167-82. Related Articles, Links

Purification of transfer factors.

Rozzo SJ, Kirkpatrick CH.

Conrad D. Stephenson Laboratory for Research in Immunology, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado.

Transfer factor activities have been studied in both clinical and basic science settings for several decades. Until now, highly purified transfer factors that are suitable for molecular analysis have not been available. This has impeded progress towards understanding the molecular and cellular basis of the activities of these important inducers of cell-mediated immune responses. Murine transfer factors with specificities for chicken egg albumin or horse spleen ferritin were purified to virtual homogeneity using a combination of affinity chromatography and reversed-phase and polytypic high performance liquid chromatography (hplc). Transfer factors prepared by this methodology were recovered in high yield and in biologically-active, antigen-specific forms. The purified materials were further analyzed using sodium dodecyl sulfate polyacrylamide gel electrophoresis, chromatographic methods and an in vivo assay for immunological activity. For the first time definitions for unit transfer factor activity and specific activity are introduced. The results of these experiments indicate that transfer factors are a family of highly polar, hydrophilic molecules of low molecular weight (approximately 5,000) which are produced in small quantities by lymphoid cells and which have potent biological activity. The availability of purified transfer factors should facilitate definitive studies into the nature and mechanisms of production and action of these molecules.

PMID: 1542296 [PubMed - indexed for MEDLINE]
Int J Biochem. 1988;20(10):1067-72. Related Articles, Links

Chromatographic and enzymatic effects on transfer factor-like activity from human leukocytes and porcine spleen dialysate.

Karhumaki E, Marnela KM, Krohn K.

Institute of Biomedical Sciences, University of Tampere, Finland.

1. The effect of dialysable transfer factor (TFd), derived from human leukocytes or porcine spleen cells, was measured using Listeria resistance in mice. 2. The molecular weight range of substance(s) containing TF-like activity is in the less than 3500 MW dialysis fraction on the basis of the capacity of peritoneal macrophages to produce superoxide anion (O2-). This biological activity is removed by heating at 56 degrees C. 3. After Sephadex G-10 chromatography of dialysates the significant activities are found in fractions III and IV of human leukocyte dialysate and in fractions of II and III of porcine spleen dialysate. 4. From enzymatic studies, most of the protective activity of both human leukocyte and porcine spleen dialysate is based on the action of small-molecular weight structures containing peptides and/or polynucleotides.
Microbiol Immunol. 1978;22(11):701-10. Related Articles, Links

In vitro assay for responsiveness of lymphocytes to transfer factor by a new leukocyte migration inhibitory test.

Miyagawa Y, Kawasaki A, Komiyama A, Akabane T.

Transfer factor (TF) causes nonimmune lymphocytes to produce leukocyte migration inhibitory factor (LMIF) in the presence of purified protein derivative (PPD). The activity of TF was measured by leukocyte migration inhibitory test (LMIT). The LMIT was a modification of the conventional agarose droplet method. To express the activity of LMIF quantitatively and simply, LMIF titer was introduced. The LMIF titer was obtained from the combination of two factors, LMIF dilution and cell migration diameter, and therefore this made the LMIT much more sensitive as compared to the conventional LMIT. The responsiveness of lymphocytes from acute lymphoblastic leukemia (ALL) and from cell-mediated immunodeficiency in children to TF was assayed by LMIT. In ALL, the lymphocyte responsiveness was poor in relapse but

improved with remission. The responsiveness was remarkably well in 3 patients with cell-mediated immunodeficiency. This method appears useful for the in vitro evaluation of responsiveness of lymphocytes to TF.

PMID: 370507 [PubMed - indexed for MEDLINE]
Proc Natl Acad Sci U S A. 1975 November; 72(11): 4573–4576.

Guinea pig transfer factor-like activity detected in vitro.
W Dunnick and F H Bach

Abstract

"Transfer factor" was prepared by Sephadex G-25 chromatography of lymph node cell lysates from guinea pigs immunized with ovalbumin or bovine gamma globulin. Treatment of nonimmune peritoneal exudate cells with the transfer factor and specific antigen leads to inhibition of migration of the cells, whereas cells treated with the transfer factor alone or specific antigen alone are not inhibited from migrating. An average of 24-28% inhibition is observed in the presence of transfer factor and specific antigen, but only 5-15% inhibition in the presence of transfer factor and nonspecific antigen. The guinea pig transfer factor we have tested in vitro has some physical characteristics in common with human transfer factor.

Full text

1: Trans Assoc Am Physicians. 1979;92:239-56.
Related Articles, Links

The chemical nature of the antigen-specific moiety of transfer factor.

Wilson GB, Paddock GV, Fudenberg HH.

PMID: 95068 [PubMed - indexed for MEDLINE]
Am J Med. 1983 Jan;74(1):161-8. Related Articles, Links

Clinical and immunologic response to antigen-specific transfer factor in drug-resistant infection with Mycobacterium xenopi.

Dwyer JM, Gerstenhaber BJ, Dobuler KJ.

The administration of transfer factor obtained from three donors who had recovered from clinical infections with Mycobacterium xenopi to a patient who had a destructive pulmonary infection with this organism, was associated with the reversal of an unfavorable clinical course. Cavitary tuberculosis associated with resistance to all combinations of antituberculosis drugs was probably related to a concurrent depression of cell-mediated immunity of unknown origin. Antigen specific but not nonspecific transfer factor caused a rapid and prolonged improvement in both the pulmonary disease and the immunologic deficiency. Cross-reactivity between the antigenic determinants of M. xenopi and Mycobacterium tuberculosis made it possible to use transfer factor obtained from donors responsive to purified protein derivative of tuberculin. This study clearly demonstrates the additional benefits to be gained from using transfer factor that is antigen-specific in the treatment of infectious diseases.

Publication Types:
• Case Reports

PMID: 6184988 [PubMed - indexed for MEDLINE]
1: J Immunol. 1976 Sep;117(3):789-96. Related Articles, Links

Human transfer factor: fractionation and biologic activity.

Burger DR, Vandenbark AA, Daves D, Anderson WA Jr, Vetto RM, Finke P.

Human transfer factor (TF) was fractionated by exclusion chromatography and the fractions were tested for biologic activity in vivo and in vitro. Specific TF activity in vivo was found to reside in the major UV-absorbing peak (Fraction III). Fraction III eluted at 2.7 X V(O) and transferred tuberculin, candida, or KLH-reactivity to previously negative recipients. Fraction III from nonreactive donors was ineffective. When the fractions were tested in vitro, we found that both the mitogenic activity of whole TF and the suppressive activity to mitogen activation when present in TF was found in Fraction

I. Fraction III contained components responsible for augmentation of PHA and PWM responses. In addition, Fraction III contained the component responsible for antigen-dependent augmentation of lymphocyte transformation. Fraction IV was suppressive to antigen-induced lymphocyte transformation. These data suggest that TF preparations contain components which can affect immune reactions in both specific and nonspecific ways.

PMID: 134121 [PubMed - indexed for MEDLINE]
Immunol. 1976 Sep;117(3):782-8. Related Articles, Links

Human transfer factor: effects on lymphocyte transformation.

Burger DR, Vandenbark AA, Finke P, Nolte JE, Vetto RM.

Transfer factor preparations from 57 different donors have been compared for effects on mitogen- and antigen-induced lymphocyte transformation. Nine of the preparations were mitogenic when added to cultured lymphocytes although the magnitude of this activity was relatively low. The majority of the preparations (48/57) did not affect PHA-induced lymphocyte transformation although augmentation (6 of 57) and suppression (3 of 57) was observed with some. In addition we observed that most of the preparations tested suppressed ConA stimulation and augmented the PWM response. When selected preparations were evaluated on antigen-responsive cells, there was a correlation between the magnitude of antigen responsiveness and the magnitude of TF augmentation of antigen-induced lymphocyte transformation (p less than 0.005). Cultures that were not responsive to antigen (KLH-negative or BUdR-treated) could not be stimulated by TF from immune donors and antigen. These data suggest that TF preparations contain either stimulatory or inhibitory components and that TF is not capable of activating naive lymphocytes to undergo transformation in response to antigen.

PMID: 956653 [PubMed - indexed for MEDLINE]
J Immunol. 1976 Sep;117(3):797-801. Related Articles, Links

Nicotinamide: suppression of lymphocyte transformation with a component identified in human transfer factor.

Burger DR, Vandenbark AA, Daves D, Anderson WA Jr, Vetto RM, Finke P.

The component in human transfer factor (TF) (Fraction IV, from exclusion chromatography on Sephadex G-25) responsible for suppression of antigen-induced lymphocyte transformation was previously identified as nicotinamide. Commercially available nicotinamide was subsequently shown to produce suppression of antigen-induced responses in vitro previously observed with TF Fraction IV. Nicotinamide was found to be nontoxic at the highest concentrations employed (10(-2)M) and suppressive over a relatively broad range (10(-5) to 10(-2)M. The suppression appeared to be related to the magnitude of antigen- or mitogen-induced transformation and was apparent even when nicotinamide was added as late as 48 hr after stimulant addition.

PMID: 134122 [PubMed - indexed for MEDLINE]
Med Biol. 1976 Dec;54(5):334-40. Related Articles, Links

Fractionation studies on human leucocyte dialyzates. Demonstration of three components with transfer factor activity.

Krohn K, Grohn P, Horsmanheimo M, Virolainen M.

Fractionation of dialyzates of human leucocyte lysates on a Sephadex G-10 column yielded seven fractions. Oidiomycin sensitivity could be induced with fractions I, III and VI in those recipients whose skin tests had previously been negative. Uraemic patients, who were skin test negative to 100 TU of PPD, regained their in vivo reactivity to PPD after receiving 5 mug of fraction VI, while no alteration in their blast transformation responses to the antigen was observed. We suggest that the active components at least in fractions III and VI, and perhaps also in fraction I, act nonspecifically by stimulating weak immune reactivity or by supporting reactions leading to the expression of this reactivity.

PMID: 994567 [PubMed - indexed for MEDLINE]
Med Biol. 1976 Dec;54(5):334-40. Related Articles, Links

Fractionation studies on human leucocyte dialyzates. Demonstration of three components with transfer factor activity.

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PMID: 994567 [PubMed - indexed for MEDLINE]
Scand J Immunol. 1977;6(11):1101-6. Related Articles, Links

Specificity of transfer factor. In vitro lymphoblast transformation of peripheral lymphocytes to Leishmania major antigen in the presence of transfer factor.

Sharma MK, Anaraki F, Ala F.

The in vivo and in vitro demonstration of specificity of transfer factor (TF) has so far been hampered by lack of a suitable antigen. The host partiality of Leishmania suggested that in the case of leishmania antigen it should be possible to obtain lymphocytes of both donors and recipients of TF which were either sensitized or truly virgin. Lymphoblast transformation of normal donor lymphocytes to leishmania major antigen (LMA) was therefore measured in the presence of TF prepared from donors with a history of cutaneous leishmania infection (LSTFd) and normal donors (NSTFd). A clear augmentation of the lymphoblast transformation equal to that usually seen when lymphocytes from sensitized individuals are exposed to LMA was observed with LSTFd. An insignificant increase in lymphoblast transformation, however, occurred when NSTFd was used together with LMA and when LSTFd or NSTFd was used alone. The results, although limited by the number of TF preparations, tested, clearly substantiate the in vitro specificity of TF.

PMID: 74087 [PubMed - indexed for MEDLINE]
Int Arch Allergy Appl Immunol. 1977;54(3):269-80. Related Articles, Links

Biologic activity of transfer factor tested in vitro with cord blood lymphocytes.

Muller MR, Grob PJ, Hitzig WH.

Cord blood lymphocytes, generally believed to be immunologically uncommitted, were used for investigating the possible conversion by transfer factor (TF) of non-immune to immune lymphocytes in vitro. TF was prepared from pooled buffy coats of normal blood bank donors by ultrafiltration and lyophilization, and it ability to influence lymphocyte transformation was assessed by measuring increases in 3H-thymidine uptake into DNA after stimulation with purified protein derivative of tuberculin and/or streptokinase-streptodornase in 23 experiments with cord blood and 15 adult controls. TF stimulated cord blood lymphocytes nonspecifically when added to the medium alone. In the presence of antigen, TF acted in a synergistic, antigen-dependent way with either amplifying or inhibitory effects in adult good responders. These effects were negligible in adult low responders and in cord blood. From our observations no specific conversion of lymphocytes by TF in vitro can be deduced.

PMID: 873625 [PubMed - indexed for MEDLINE]
J Allergy Clin Immunol. 1976 Jul;58(1 PT. 2):190-7. Related Articles, Links

Transfer factor: hypoxanthine is a major component of a fraction with in vivo activity.

Tomar RH, Knight R, Stern M.

Transfer factor was prepared from the leukocyte lysates of four donors with known skin test reactivity. After ultrafiltration and double-gel filtration on polyacrylamide gels, fraction IV of the preparation was found to have biologic activity. This fraction contained one major and occasionally one minor ultraviolet-absorbing and zero to one ninhydrin-detectable spots on thin-layer chromatography. The major ultraviolet spot was identified as hypoxanthine. Hypoxanthine was demonstrated to be responsible for the high 260 nm/280 nm ratio of preparations with biologic activity in vivo. It was not determined if hypoxanthine is required for transfer factor activity. In addition, an orcinol-negative preparation also had biologic activity.

PMID: 956555 [PubMed - indexed for MEDLINE]
J Allergy Clin Immunol. 1976 Jul;58(1 PT. 2):190-7. Related Articles, Links

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PMID: 956555 [PubMed - indexed for MEDLINE]
Acta Paediatr Scand. 1977 Mar;66(2):219-24. Related Articles, Links

Transfer factor and cellular immune response in urinary tract infections in children.

Anttila R, Grohn P, Krohn K.

Cellular immune responses in vivo and in vitro were studied in 20 children with chronic or relapsing urinary tract infections. Skin tests revealed decreased immune responses to PPD in cases with chronic or recurrent pyelonephritis and to OM, in these cases and in cases of lower urinary tract infections. Blast transformation responses to PPD, OM and PHA were at least as high as in controls. Administration of chromatographically purified fraction from human leucocyte transfer factor resulted in a positive skin reaction with antigen concentration, which before TF administration had caused a negative reaction. The results suggest that the action of the transfer factor component used in this study is based on an immunologically nonspecific stimulation of the cellular immune response.

Publication Types:
• Clinical Trial

PMID: 320817 [PubMed - indexed for MEDLINE]
Probl Med Wieku Rozwoj. 1990;16:167-88. Related Articles, Links

[Transfer of delayed type hypersensitivity in guinea pigs]

[Article in Polish]

Smogorzewska E.

Instytut Matki i Dziecka.

In the first description of transfer factor in 1955, Lawrence defined it as "the active principle in viable leukocytes, leukocyte extracts and leukocyte dialysates obtained from immune human donors which has the capacity to transfer cutaneous delayed-type hypersensitivity (DTH) in vivo to nonimmune recipients". The dialysates are reported to contain a number of antigen-independent activities affecting monocytes, macrophages and lymphocytes. In some cases these "nonspecific" activities separate out with the fraction causing skin test conversion, but it has not been shown that the same molecule is responsible for both effects. Chemical structure of transfer factor (TF) has not been defined, yet. Its m.w. is 2000-3500. TF has been used to treat a wide range of clinical disorders, including immunodeficiency diseases, neoplasms, chronic fungal, viral and bacterial infections with varying degrees of reported success. The reports on the efficacy of TF in the prevention of varicella in childhood leukemia evoked renewed interest in possible clinical applications of this leukocyte derived material. There is no convenient animal in vivo model of TF activity investigations, and there is no sensitive and reproducible in vitro assay in regard to its activity and specificity. In presented paper the passive transfer of DTH to tuberculin in guinea pigs was reported, both by intact lymphocytes as well as by its crude homogenate. Sephadex column fractionation of crude leukocyte extract have been done. Attempts to define the in vitro activity of leukocyte extract as well as its fractions by leukocyte migration inhibition test have been made.

PMID: 2152405 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1977 Mar;27(3):416-20. Related Articles, Links

In vitro effect of transfer factor on active rosettes and leucocyte migration of patients with cancer.

Nekam K, Kalmar L, Gergely P, Kelemen G, Fekete B, Lang 2, Levai J, Petranyi GY.

The in vitro effect of transfer factor (TF) and its obtained by gel filtration was studied on the active rosettes and leucocyte migration inhibition. TF and one fraction (IV) restored the reactivity of lymphocytes from tumour-bearing patients to tuberculin and Candida antigens in the leucocyte migration assay. TF and fraction IV was also found to enhance the

number of active rosettes of tumour-bearing patients, whereas no such effect was observed on lymphocytes of patients with active SLE or controls.

PMID: 324669 [PubMed - indexed for MEDLINE]
Trop Med Parasitol. 1986 Dec;37(4):399-402. Related Articles, Links

Dialyzable transfer factor in experimental Chagas' disease: in vitro studies.

Machado RZ, Laure CJ, De Lucca FL.

The dialyzable transfer factor (TF) was prepared from spleen and lymph node cells of either normal (TFn) or infected (TFi) mice with Trypanosoma cruzi. The ability of TFn and TFi in transferring cellular immunity to T. cruzi antigens was assessed by the macrophage migration inhibition assay and lymphocyte transformation test. The results obtained with these two immunological assays indicated that only TFi is able to transfer cellular immune responses. This phenomenon was antigen specific. The content of free amino acids in TFi preparation was higher than in TFn. However, our data indicated that the stimulation of lymphocyte transformation is not due to the increase in glycine and serine. This activity of TFi required the addition of T. cruzi antigens. Our findings support the hypothesis that TFi is derived from immune RNA.

PMID: 3105040 [PubMed - indexed for MEDLINE]
Int Arch Allergy Appl Immunol. 1978;57(3):210-20. Related Articles, Links

The effect of transfer factor on lymphocyte transformation. Comparison of augmentation by dialysates of leucocytes and lymphoid and non-lymphoid organs.

Uotila A, Hamblin A, Dumonde DC, Krohn KJ.

In this paper we describe experiments to determine whether dialysable extracts of non-lymphoid and lymphoid organs augment lymphocyte transformation in vitro in a manner similar to the augmenting activity of leucocyte dialysates. Human peripheral blood leucocytes were cultured with tuberculin PPD or leucoagglutinin, and dose-related effects of the dialysable extracts on lymphocyte transformation were studied by 125IUdR incorporation. Augmentation of lymphocyte transformation was obtained not only with leucocyte dialysates but also with dialysable extracts of lymphoid and non-lymphoid organs (e.g. spleen, liver, kidney, brain). It is concluded that the agent or agents present in dialysable leucocyte transfer factor preparations, which augment lymphoid transformation in vitro, are widely distributed throughout mammalian tissues.

PMID: 659013 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1984 Jan-Feb;12(1):1-5. Related Articles, Links

Transfer factor--a lymphocyte cell surface component.

Schroder I, Luneburg S.

An attempt was made to locate the biologically active component of the DLE in lymphocytes. The test was based on the recovery of sheep cell-rosetting capacity in trypsinized human lymphocytes (recovery assay). Comparisons of the extract from trypsinized leukocytes and the leukocyte supernatant (after trypsination) yielded the following results: The peptide fraction detached from the cell surface by trypsin (30 min with 0.5 g trypsin/l at 37 degrees C) accounts for most of the TF activity of the whole lymphocytes. Of the two TF activities (fractions II and III), fraction III obviously stems from the cell interior because it cannot be liberated by trypsin. Fraction III is characterized by an unusually high UV absorption quotient (A 260/280), probably due to a large nucleotide content. Trypsination leads to the biologically active TF fraction going into the supernatant. Fraction II consists almost entirely of cell surface peptides. It is relatively easy to separate it cleanly, and it has a high level of biological activity (1 microgram/ml is still detectable).

PMID: 6731201 [PubMed - indexed for MEDLINE]
Ann Allergy. 1976 May;36(5):330-6. Related Articles, Links

Increase in E-rosettes after transfer factor (TF) treatment: fractionation of TF.

Khan A, Thometz D, Garrison O, Hill JM.

The effect of transfer factor (TF) on E-rosettes (ER) was studied in vivo in a patient with Hodgkin's disease. Transfer factor was given in doses of 10 units/sq m intramuscularly. The ER forming cells and the ER scores were determined. The

ER score method took into account the number of erythrocytes in each rosette. The increase in ER score was maximum at 24 hours and it declined during the following one to two weeks. It was suggested that TF may have to be given more frequently than indicated by the persistence of skin reactivity. TF was fractionated with high pressure liquid chromatography. Fraction 2 increased ER in a patient with Schwannoma. Non-specificity of TF was also discussed.

Publication Types:
• Case Reports

Poult Sci. 1983 May;62(5):767-71. Related Articles, Links

Adoptive transfer of delayed wattle reactivity in chickens with a dialyzable leukocyte extract containing transfer factor.

Giambrone JJ, Klesius PH, Yu M.

Delayed wattle reactions (DWR) to tuberculin, diphtheria toxoid (DT), and keyhole limpet hemocyanin (KLH) were transferred to chickens with dialyzable leukocyte extracts (DLE) prepared from splenic leukocytes of chickens sensitized and reactive by DWR to the tuberculin, DT, or KLH. A DLE prepared from chickens unsensitized and unreactive to tuberculin by DWR failed to transfer DWR to tuberculin in recipients. Only chickens injected with DLE from tuberculin sensitized and reactive chickens exhibited significant (P less than .01) DWR to tuberculin. Chickens that received DLE prepared from DT sensitized and reactive chickens exhibited significant (P less than .01) DWR to DT but not to KLH. Further, DWR to both DT and KLH was transferred with DLE prepared from chickens sensitized to both antigens. Adoptive transfer of DWR to KLH in comparison to DT was more successful. Finally, the serial transfer of DWR to KLH (P less than .05) but not to DT (P greater than .05) was accomplished using DLE prepared from chickens that previously were recipients of DLE prepared from chickens sensitized to KLH and DT. Results indicate that DLE prepared from chickens contain transfer factor (TF) responsible for adoptive transfer of DWR to tuberculin, DT, and KLH.

PMID: 6878121 [PubMed - indexed for MEDLINE]
Z Immunitatsforsch Immunobiol. 1977 Dec;153(5):395-411. Related Articles, Links

Studies on the chemical composition and biological properties of transfer factor.

Krohn K, Uotila A, Vaisanen J, Grohn P.

Dialyzable transfer factor (dTF) was fractionated on Sephadex G-10 and G-25 fine columns, and biological activity was found in 3 fractions. One of these, designated VIa, and having a tendency to adsorb to the Sephadex G-10 gel, was shown to have a therapeutic effect on certain immunological diseases. Analysis of this fraction on thin-layer and gas chromatography and with infrared and mass spectroscopy indicated that about half of this fraction was composed of uracil; additional unidentified heterocyclic and aromatic substances were present in this fraction. Adjacent fraction V contained tyrosine and a small polyribonucleotide, and fraction VII hypoxanthine and additional unidentified components. Our results suggest that the therapeutic activity of dTF is not mediated through an immunologically specific informational molecule, but is rather based on non-specific stimulation of the expression of the immune response.

PMID: 602344 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1982 May-Jun;10(3):171-6. Related Articles, Links

In vitro determination of effects of dialyzable leukocyte extracts containing transfer factor activity.

Schroder I, Rovensky J.

The studies for determining the effects of dialyzable leukocyte extracts (transfer factor) as reflected in recovery of E-rosetting capacity in trypsinised lymphocytes (recovery-assay) suggested the following: 1. Dialyzable leukocyte extracts contain an inhibitor with a molecular weight of about 5000 (fraction I). 2. This inhibitor considerably affects the immunologic activity of both whole preparations and their different fractions during the in vitro activity assay. 3. The inhibitor fraction that fails to respond to the "recovery-assay" (less than 5%) responds very actively to the test after inactivation (45 min/57 degrees C). 4. Therefore, activation assays performed on the total preparation after inactivation involve a considerable error. 5. Immunological activity is concentrated in fractions III and IV. Only fraction III activity can be reduced considerably by inactivation. Fraction II activity is induced by incomplete separation from fraction III. Fraction IV cannot be inactivated. 6. In the case of transfer factor preparations (without inhibitor fractions) activity increases almost in direct proportion to the concentration up to about 30 micrograms. 7. Since the "recovery-assay" also responds to substances with no immunologic activity, its use can be justified in the case of fraction III. The activity is then the difference between the native and the inactivated forms. 8. A corresponding review of methods (such as LTT, migration inhibition test, skin test, etc.) currently used for activity assays seems advisable.

PMID: 7148610 [PubMed - indexed for MEDLINE]
Allergy Clin Immunol. 1978 Feb;61(2):115-8. Related Articles, Links

Skin test conversion following transfer factor. A double-blinded study of normal individuals.

Neidhart JA, Christakis N, Metz EN, Balcerzak SP, LoBuglio AF.

The use of skin test conversion as a measure of change in cellular immune status is a fairly routine procedure despite considerable potential for variation in testing. This study is a double-blinded and randomized reassessment of this assay in the context of transfer factor (TF) activity. Thirty-three normal people with negative tuberculin skin tests received either dialyzable TF, column purified TF, hypoxanthine, or saline in a randomized and double-blinded fashion. Skin test reactivity to tuberculin and keyhole limpet hemocyanin (KLH) was read by three of the investigators. Nine of 20 recipients of TF and 7 of 13 controls demonstrated an increase in tuberculin reactivity after "transfer." Four reactions were greater than 10 mm. Fourteen of 20 recipients of TF and 7 of 13 controls demonstrated some reactivity to KLH on initial testing post-transfer. Control solutions were as effective as TF preparations in "causing" skin test conversion. These observations stress the importance of controlled and and blinded studies when serial skin test reactivity is used to evaluate cellular immune status in humans.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial
Dev Biol Stand. 1986;58 (Pt B):531-44. Related Articles, Links

Dialyzable tuberculins: their abilities to participate in or inhibit immune reactions.

Chaparas SD, Godet K, Ally DB, Holobaugh P.

Dialyzable components of culture filtrate of Mycobacterium bovis were fractionated by gel filtration on Sephadex G-10 into eight fractions, A through H in order of their elution from the column. None of the fractions produced a visible precipitate when reacted with a hyperimmune antiserum. The first five fractions were further investigated. All were capable of inhibiting precipitation of nondialyzable tuberculin. Fraction E, containing the smallest fragments, totally abolished precipitation and fraction A, which contained the largest molecules inhibited the least. Fractions A and B were the only ones that could induce skin reactions in sensitized guinea pigs but did this poorly. In vitro transformation of PPD sensitized lymphocytes was induced only by fraction A. Only fractions A and B could inhibit transformation of lymphocytes by Concanavalin A but only fraction B could inhibit transformation by tuberculin. Dialyzable components injected intracardially 3 hours prior to skin testing with tuberculin caused a reduction in skin reactivity. Since such substances are present in tissues in late stages of tuberculosis investigations were made to determine if they played a role in the induction of the observed accompanying tolerance to skin test cellular hypersensitivity. Guinea pigs treated with dialyzable components prior to and for four weeks post sensitization did not develop tolerance.

PMID: 3301462 [PubMed - indexed for MEDLINE]
Acta Virol. 1987 Nov;31(6):449-57. Related Articles, Links

Nature and antigen-specific activities of transfer factor against herpes simplex virus type 1.

Huang LL, Su CZ, Wan ZF.

Dpt. of biochemistry, Fourth Military Medical College, Xian, China.

Transfer factor specific for herpes simplex virus (HSV) type 1 (TFHSV-1) was prepared from splenic cells of HSV-1 immunized mice. Protection was transferred with TFHSV-1 to nonimmune mouse recipients. The TFHSV-1 injected mice had a higher survival rate after lethal HSV-1 challenge as compared to mice injected with a nonspecific transfer factor (P less than 0.05). 51Cr-labelled leukocyte adherence inhibition (51-Cr-LAI) test was used to demonstrate the specific activity of transfer factor in vitro. Only leukocytes incubated with TFHSV-1 exhibited significant adherence inhibition (P less than 0.01) to HSV-1 antigen, but not to control antigen. Specific activity component of TFHSV-1 (STFc) was separated by affinity adsorption with the antigen. Activity of STFc in 51Cr-LAI test was significantly higher than that of TFHSV-1 (P less than 0.01). Ratio activity of STFc in protective host immunity was 16 times as much as that of TFHSV-1. STFc was analysed by high performance liquid chromatography, thin layer chromatography and isoelectric focusing in the polyacrylamide gel. Results revealed that STFc appeared to be a polypeptide with a molecular weight of about 12,870 dalton.

PMID: 2449810 [PubMed - indexed for MEDLINE]
Acta Virol. 1987 Nov;31(6):449-57. Related Articles, Links

Nature and antigen-specific activities of transfer factor against herpes simplex virus type 1.

Huang LL, Su CZ, Wan ZF.

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PMID: 2449810 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1987 May-Jun;15(3):143-4. Related Articles, Links

Effect of different fractions of dialyzable leukocyte extract--transfer factor--on the chemiluminescence of human phagocytes.

Sipka S, Schroder I, Brazsnikova NA.

3rd Department of Medicine, University Medical School, Debrecen, Hungary.

The chemiluminescence (CL) inducing effect of the fractions of dialyzable leukocyte extract (DLE)--transfer factor--from tonsil leukocytes was tested on the phagocytes of human whole blood. The fractionation of DLE by Sephadex G-25 results in three main fractions: I, II, III. We found only fraction II having a direct CL inducing effect on the non-stimulated cells. Fraction II increased further the CL of phagocytes which were stimulated by zymosan (Mannozym). Fractions I and III were ineffective. We suggest that in the complex "transfer factor" effects of DLE, the stimulation of the peripheral phagocytes of blood-by the oligopeptides of fraction II may have an important role.

PMID: 3661353 [PubMed - indexed for MEDLINE]
Bull Tokyo Med Dent Univ. 1989 Sep;36(3):35-40. Related Articles, Links

Effects of dialyzable leukocyte extracts (DLE) and inosine on stimulated lymphocytes.

Komatsu F.

Blood Transfusion Service, School of Medicine, Tokyo Medical and Dental University.

The effects of dialyzable leukocyte extracts (DLE) on the lymphocytes were examined. The crude DLE suppressed the blast-formation of the PHA-stimulated lymphocytes and proliferation of the leukemic cell-lines but enhanced that of the fibroblastic cells. A certain fraction of the DLE caused the ATP level of the stimulated lymphocytes to rise, after incubation for 24 hours. The fraction was further purified and the inosine eluted from it. The inosine increased the ATP level and markedly enhanced the lymphocyte blast-formation and proliferation of the fibroblastic cells and leukemic cell-lines. It is suggested that when the DLE show some effects on the lymphocytes, the inosine contained in the DLE may show important effects. The effect of inosine was inhibited by other substances contained in the DLE, especially deoxynucleotides. These substances suppressed the blast-formation of the lymphocytes and the proliferation of the leukemic-cell lines. It remains to determine why the fibroblastic cells were not suppressed by them.

PMID: 2632132 [PubMed - indexed for MEDLINE]
Immunol Lett. 2000 Nov 1;74(3):201-5. Related Articles, Links

Differences in the changes of allergen-specific IgE serum levels and the chemiluminescence of peripheral blood phagocytes in patients with allergic rhinoconjunctivitis during the ragweed season.

Szabo Z, Szilasi M, Brugos L, Szanto S, Kovacs I, Szeles M, Lakos G, Antal-Szalmas P, Edes I, Sipka S.

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The objective of this study was to compare the changes in the values of allergen-specific serum IgE levels and zymosan-induced whole blood chemiluminescence (CL) in 41 patients who had exclusively only ragweed allergy in the season of acute symptoms of disease in July, August and September. All patients had allergic rhinitis or rhinoconjunctivitis. Each patient was investigated as a self-control. The ragweed-specific IgE levels were measured by enzyme immunoassay (EIA). The luminol amplified zymosan-induced CL of whole human blood was detected. The allergen-specific serum IgE levels showed slight, but not significant, gradually increasing elevations during the whole season. On the other hand, significant increases were found in the values of the basal but especially in the zymosan-stimulated CL of peripheral blood phagocytes during the acute phase of allergy. Both the basal and the zymosan-induced CL reflected significantly the activated state of the immune system. These observations clearly show that there are well detectable signs of the systemic activation of the immune system in allergic rhinoconjunctivitis beside the local alterations. In addition, the measurements of the basal and zymosan-induced CL of peripheral phagocytes could clearly reflect the clinical state of disease in vitro.
Acta Pathol Microbiol Immunol Scand [C]. 1987 Dec;95(6):251-6. Related Articles, Links

Effect of leukocyte and other tissue dialysates on NBT reduction and prostaglandin production in mice.

Karhumaki E.

Department of Biomedical Sciences, University of Tampere, Finland.

The effects of human leukocyte, porcine spleen and bovine liver dialysate fractions on Listeria resistance were measured by survival studies and by assessing the capacity of peritoneal macrophages to produce superoxide anion (0-2) and prostaglandins. Leukocyte (DLE) and other tissue dialysates were fractionated on a Sephadex G-10 column. Thereafter the significant activities were found in fraction III of DLE, fraction II of porcine spleen and fraction II + III of bovine liver dialysate. The treatment with active porcine spleen dialysate fraction increased the capacity of peritoneal macrophages to generate superoxide anion. On the other hand, this fraction significantly decreased the production of prostaglandin PGE2 and thromboxan B2. These results may indicate that all dialysates can be a source of a non-specifically-acting immunomodulatory preparation and that the infection-resistance-increasing substances seem to operate via the monocyte/macrophage activation.

PMID: 2831694 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):171-4. Related Articles, Links

The effect of DLE fractions on GM-progenitors of haematopoietic stem cells in vitro.

Barnet K, Vacek A, Cech K, Pekarek J.

SEVAC a.s., Praha, Czech Republic.

Dialysable leucocyte extract (DLE) prepared from buffy coats of human blood, potentiates the effect of Colony-stimulating factor (CSF) on the growth of granulocyte-macrophage colony forming cell (GM-CFC) colonies in vitro. This relative increase of the number of colonies is apparent when diluted CSF (present in lung conditioning medium) as a control, and DLE, in a wide range of concentrations are added to the culture of mouse bone marrow cells. Fractionation of DLE on Amicon membranes revealed that the activity resides in molecules of 0-5 kD. Molecules 5-10 kD have no potentiating effect. DLE and its fractions (0-5 kD, 0-1 kD), except fractions 0-500 D and 5-10 kD, when added undiluted i.e. at the initial concentration, exerted a suppressive effect: colonies are not formed despite the presence of CSF. In a pilot experiment, it was shown that DLE is able to stimulate colony-forming activity of earlier progenitors of erythroid cells (BFUe), under the influence of erythropoietin.

PMID: 8993777 [PubMed - indexed for MEDLINE]
Biochem Biophys Res Commun. 2000 Jul 14;273(3):1099-103. Related Articles, Links

Dialyzable leukocyte extract suppresses the activity of essential transcription factors for HIV-1 gene expression in unstimulated MT-4 cells.

Ojeda MO, Fernandez-Ortega C, Rosainz MJ.

Cell Biology Division, Center for Biological Research, Havana, Cuba.

The human immunodeficiency virus type 1 (HIV-1) contains regulatory regions in its long terminal repeat (LTR) implicated in the control of viral gene expression. We previously demonstrated that Dialyzable Leukocyte Extract (DLE), a preparation derived from immune leukocytes, is able to inhibit HIV-1 replication in MT-4 cell cultures. Here, we examined the effect of DLE on the activation of NF-kappaB and Sp1 transcription factors. NF-kappaB activity was completely suppressed after seven days of treatment with 2.5 U/mL of DLE, with a parallel large reduction in the amounts of Sp1 complexes. These findings correlate with the maximum inhibitory effect on HIV-1 replication described in a previous report. IkappaBalpha and NF-kappaB p65(RelA) gene expression are not regulated by DLE in MT-4 cells. Although up to day, the precise molecular mechanism of DLE biological activity in HIV-1 infection remains unclear, this report presents data that indicate a potential downregulatory effect of DLE on HIV-1 gene expression.

PMID: 10891378 [PubMed - indexed for MEDLINE]
Miriam Ojeda Ojeda, Celia Fernández-Ortega and Manuel de J. Arana Rosaínz

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Abstract
The human immunodeficiency virus type 1 (HIV-1) contains regulatory regions in its long terminal repeat (LTR) implicated in the control of viral gene expression. We previously demonstrated that Dialyzable Leukocyte Extract (DLE), a preparation derived from immune leukocytes, is able to inhibit HIV-1 replication in MT-4 cell cultures. Here, we examined the effect of DLE on the activation of NF- B and Sp1 transcription factors. NF- B activity was completely suppressed after seven days of treatment with 2.5 U/mL of DLE, with a parallel large reduction in the amounts of Sp1 complexes. These findings correlate with the maximum inhibitory effect on HIV-1 replication described in a previous report. I B and NF- B p65(RelA) gene expression are not regulated by DLE in MT-4 cells. Although up to day, the precise molecular mechanism of DLE biological activity in HIV-1 infection remains unclear, this report presents data that indicate a potential downregulatory effect of DLE on HIV-1 gene expression.
Author Keywords: transfer factor; immunodeficiency; HIV-1; AIDS; NF- B

Biochemical and Biophysical Research Communications
Volume 273, Issue 3 , 14 July 2000, Pages 1099-1

1: Allergol Immunopathol (Madr). 1989 Jan-Feb;17(1):35-7. Related Articles, Links

Transfer factor therapy of thoracic sarcoidosis.

Vezendi S, Schroder I.

Heart and Lung Department, University Medical School, Debrecen, Hungary.

The authors repeatedly treated 59 patients with thoracic sarcoidosis with transfer factor (TF) since 1976. They utilized this therapy with TF from human tonsil lymphocytes (TFh) on account of the ineffectiveness of the corticosteroid treatment, because of the side effects of the corticosteroids, and as primary TF therapy, and to test an animal TF preparation from pig tonsil lymphocytes (TFp). In their observations only fraction II of the dialysable leukocyte extract was sufficient. Differences in the effectiveness between TFh and TFp do not exist on the whole. Our conclusion is that TF can stimulate the immunosystem of the patients, and can be an important mode of treatment. The mode of action is not clear.

PMID: 2750639 [PubMed - indexed for MEDLINE]
1: Sci Sin [B]. 1985 Apr;28(4):394-401. Related Articles, Links

The study of human transfer factor.

Li ZL.

In this paper, the study of human transfer factor is reported. We established a negative pressure dialysis method instead of ordinary dialysis for treatment of the crude leukocyte extract. Dialysate is rapidly obtained in only 5 h so that a large volume of preparation is easier to handle and the chance of contamination avoided. When human TF was incubated with human cord blood T-lymphocytes and pig lymphocytes, a very high biological activity on SRBC rosette enhancement and an increase in electrophoresis rate appeared. It suggests that these assays may be used as in vitro method of evaluation of TF activity. In our clinic, TF has been in clinical trials for 5 years and has now been administered to a large number of patients with a variety of diseases, in which cell-mediated immune responses have been compromised. We observe that TF has served an efficient immunopotentiating or immunomodulation agent.

PMID: 4012263 [PubMed - indexed for MEDLINE]
N Z Med J. 1977 Jan 12;85(579):3-6. Related Articles, Links

Transfer factor therapy: clinical experience and the role of the E rosette assay.

Sutherland DC, Wilson JD, Douglas R.

Transfer factor has been administered to 17 patients, most with infectious diseases of various kinds. In 12 patients the therapy was followed by a definite clinical improvement although in most cases conventional chemotherapy was given concomitantly. In all cases where clinical improvement followed the sheep red cell or E rosette assay showed low values initially, with an improvement following therapy. This test of T lymphocyte function may be useful both in predicting patients likely to respond to transfer factor, and in monitoring response to treatment. As no specific assay of transfer factor activity is available, an in vivo rise in E rosette formation following transfer factor administration serves as a crude indicator that the injected material has some biological activity.

PMID: 319390 [PubMed - indexed for MEDLINE
Arch Med Res. 1995;26 Spec No:S87-92. Related Articles, Links

Immunotherapy with transfer factor of recurrent herpes simplex type I.

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.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 8845664 [PubMed - indexed for MEDLINE]
Presse Med. 1984 Mar 3;13(9):537-40. Related Articles, Links

[Treatment of herpes infections with transfer factor]

[Article in French]

Rosenfeld F, Viza D, Phillips J, Vich JM, Binet O, Aron-Brunetiere R.

Twelve patients suffering from recurrent herpetic infections resistant to several current therapies were treated for a 3 to 10 months period with a bovine transfer factor specific to Herpes simplex virus of type 1 and 2. The results obtained showed that this treatment was capable of dramatically reducing the intensity, duration and frequency of the relapses. This preliminary clinical trial suggests that specific transfer factor administered orally could be an effective treatment of herpes infections.

Publication Types:
• Clinical Trial

PMID: 6230646 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):73-5. Related Articles, Links

Effect of anti-herpes specific transfer factor.

Byston J, Cech K, Pekarek J, Jilkova J.

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Using a blood cell separator, lymphocytes were collected from otherwise healthy convalescents suffering from herpetic infections. A specific anti-herpes dialysate (AH-DLE) was prepared from the lymphocytes, using standard procedures. Patients with recurrent herpetic infections were treated with a single dose of the dialysate, at the initial signs of herpetic infection (group A), with two doses (group B) or with three doses (group C). A total number of 37 patients (29 women, 8 men, age range 15-73 years) were treated. No improvement was observed in 7 patients (18.9%), whilst 7 patients did not manifest any exacerbation of their herpetic infection in the course of the one-year follow-up. The remaining 62.2% of the patients showed a marked improvement: decrease of the frequency and/or duration or relapses. Before AH-DLE administration, the mean number of herpes relapses in this group of patients was 12 p.a.. After therapy, the number of relapses decreased to 3.5 p.a.. No statistically significant difference was observed between groups A and B. The least favourable results were registered in group C. However, this group included 6 female patients extremely resistant to the previously therapeutic attempts, including inosiplex, non-specific DLE or acyclovir. Thus, even in this group, the therapy was successful in 50% of the patients.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 8993761 [PubMed - indexed for MEDLINE]
Int J Immunopharmacol. 1998 Oct;20(10):521-35. Related Articles, Links

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

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.

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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.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 9839657 [PubMed - indexed for MEDLINE]

Biotherapy. 1996;9(1-3):81-6. Related Articles, Links

Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome (CFS). Two case reports.

Ablashi DV, Levine PH, De Vinci C, Whitman JE Jr, Pizza G, Viza D.

Advanced Biotechnologies Inc., Columbia, MD 21046, USA.

Specific Human Herpes virus-6 (HHV-6) transfer factor (TF) preparation, administered to two chronic fatigue syndrome patients, inhibited the HHV-6 infection. Prior to treatment, both patients exhibited an activated HHV-6 infection. TF treatment significantly improved the clinical manifestations of CFS in one patient who resumed normal duties within weeks, whereas no clinical improvement was observed in the second patient. It is concluded that HHV-6 specific TF may be of significant value in controlling HHV-6 infection and related illnesses.

Publication Types:
• Case Reports

PMID: 8993763 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):87-90. Related Articles, Links

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

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.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 8993764 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):77-9. Related Articles, Links

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

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.

Publication Types:
• Review
• Review, Tutorial

PMID: 8993762 [PubMed - indexed for MEDLINE]

Biotherapy. 1996;9(1-3):91-5. Related Articles, Links

The influence of age on transfer factor treatment of cellular immunodeficiency, chronic fatigue syndrome and/or chronic viral infections.

Hana I, Vrubel J, Pekarek J, Cech K.

Dept. of Immunology, Institute for Clinical and Experimental Medicine, Prague, Czechia.

A group of 222 patients suffering from cellular immunodeficiency (CID), frequently combined with chronic fatigue syndrome (CFS) and/or chronic viral infections by Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV), were immunologically investigated and treated with transfer factor (TF). The age range was 17-77 years. In order to elucidate the influence of aging on the course of the disease and on treatment, 3 subgroups were formed: 17-43 years, 44-53 years, and 54-77 years. Six injections of Immodin (commercial preparation of TF by SEVAC, Prague) were given in the course of 8 weeks. When active viral infection was present, IgG injections and vitamins were added. Immunological investigation was performed before the start of therapy, and subsequently according to need, but not later than after 3 months. The percentages of failures to improve clinical status of patients were in the individual subgroups, respectively: 10.6%, 11.5% and 28.9%. The influence of increasing age on the percentage of failures to normalize low numbers of T cells was very evident: 10.6%, 21.2% and 59.6%. In individuals uneffected by therapy, persistent absolute lymphocyte numbers below 1,200 cells were found in 23.1%, 54.5% and 89.3% in the oldest group. Statistical analysis by Pearson's Chi-square test, and the test for linear trend proved that the differences among the individual age groups were significant. Neither sex, nor other factors seemed to influence the results. The results of this pilot study show that age substantially influences the failure rate of CID treatment using TF. In older people, it is easier to improve the clinical condition than CID: this may be related to the diminished number of lymphocytes, however, a placebo effect cannot be totally excluded.

Publication Types:
• Clinical Trial

PMID: 8993765 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):41-7. Related Articles, Links

Preliminary observations using HIV-specific transfer factor in AIDS.

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.

Publication Types:
• Clinical Trial
• Clinical Trial, Phase I

PMID: 8993756 [PubMed - indexed for MEDLINE]
Med Pediatr Oncol. 1979;6(4):295-301. Related Articles, Links

A study of transfer factor for opportunistic infections in cancer patients.

Ketchel SJ, Rodriguez V, Stone A, Gutterman JU.

Although supportive care during therapy of patients with malignancies has improved, infection remains the major cause of death in these patients. The problem of "opportunistic" infections is becoming more apparent as better antibiotics are found. The control of these infections depends in part on mechanisms of cell-mediated immunity. It has been demonstrated that delayed-type hypersensitivity can be transferred from one person to another. Therefore, we used

transfer factor in the treatment of 15 patients, most with leukemia, who had fungal, viral, or mycobacterial infections that were not responding to conventional therapy. Seven of ten evaluable patients had therapeutic control of their infections while receiving transfer factor. Transfer factor appears to have contributed to these clinical improvements and is a modality of treatment that deserves further investigation.

PMID: 225647 [PubMed - indexed for MEDLINE]
Am J Med. 1994 Nov;97(5):493-4. Related Articles, Links

Comment on:
• Am J Med. 1993 Feb;94(2):197-203.

Treatment for chronic fatigue syndrome.

Fudenberg NH.

Publication Types:
• Comment
• Letter

PMID: 7848475 [PubMed - indexed for MEDLINE]
JAMA. 1977 Aug 22;238(8):869-71. Related Articles, Links

Treatment of BechУЇet's syndrome with transfer factor.

Wolf RE, Fudenberg HH, Welch TM, Spitler LE, Ziff M.

Six patients with Behcet's syndrome were treated with transfer factor (TF) from randomly selected donors. Mucocutaneous symptoms and signs were predominant at the time that TF injections were started. Three patients showed great improvement, one moderate improvement, and one was unresponsive to multiple injections of TF from different donors. One case was uninterpretable because of concomitant administration of high doses of prednisone and chlorambucil and brief treatment with TF. These results indicate that TF therapy may be beneficial in some patients with Behcet's syndrome and that a trial of TF is warranted at least in the absence of severe ocular or neurologic manifestations.

Publication Types:
• Case Reports

PMID: 577975 [PubMed - indexed for MEDLINE]
Ital J Neurol Sci. 1984 Mar;5(1):93-6. Related Articles, Links

BehУЇet syndrome: report of two early-onset cases treated with transfer factor.

Franzoni E, Masi M, Conte R, Giovannini A, Malferrari C, Scanabissi E, Specchia F, Ricci G.

Report of two cases of Behcet syndrome in children, one with the features of a neuro-Behcet syndrome and the other with chiefly severe ocular changes. Both children were treated with transfer factor when previous treatment had proved ineffective. Some years after the beginning of treatment, which is still continuing, transfer factor may be said to be of value in Behcet syndrome.

Publication Types:
• Case Reports

PMID: 6735695 [PubMed - indexed for MEDLINE]
Lancet. 1980 Nov 1;2(8201):931-4. Related Articles, Links

Transfer factor in treatment of multiple sclerosis.

Basten A, McLeod JG, Pollard JD, Walsh JC, Stewart GJ, Garrick R, Frith JA, Van Der Brink CM.

A 2-year prospective double-blind trial of the treatment of multiple sclerosis patients with the leucocyte extract, transfer factor (TF), obtained from leucocytes of relatives living with the patient, was conducted. 60 patients with definite MS, of

whom 58 completed the trial, were divided into two equal groups, one of which received TF and the other placebo. The groups were evenly balanced with respect to sex ratios, disability, duration of disease, ratio of moderate to severe cases, and HLA phenotype. Neurological, electrophysiological, and immunological assessments were done at the start of the trial and every 6 months thereafter. The results indicated that (1) TF retarded but did not reverse progression of the disease; (2) a significant difference between treatment and placebo groups was not apparent with 18 months after the start of the trial; and (3) treatment was effective only in those patients with mild to moderate disease activity.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 6107585 [PubMed - indexed for MEDLINE]
Lancet. 1978 Apr 22;1(8069):851-3. Related Articles, Links

Long-term transfer-factor treatment for multiple sclerosis.

Fog T, Pedersen L, Raun NE, Kam-Hansen S, Mellerup E, Platz P, Ryder LP, Jakobsen BK, Grob P.

In groups of 16 patients with multiple sclerosis, 13 months' double-blind treatment with transfer factor from random normal donors differed from placebo treatment only in producing a temporary restoration of lymphocyte reactivity to measles virus antigen, and did not arrest the degeneration of nerve tissue.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 76798 [PubMed - indexed for MEDLINE]
Neurology. 1986 Oct;36(10):1399-402. Related Articles, Links

Transfer factor therapy in multiple sclerosis: a three-year prospective double-blind clinical trial.

Van Haver H, Lissoir F, Droissart C, Ketelaer P, Van Hees J, Theys P, Vervliet G, Claeys H, Gautama K, Vermylen C, et al.

One hundred five patients with MS were divided into three groups matched for age, sex, and disability, and treated with either placebo, transfer factor prepared from leukocytes of random donors, or transfer factor from leukocytes of family members living with the patients. There were no differences in the three treatment groups for changes in disability, activities of daily living, or evoked potentials. Eighteen months of transfer factor therapy had no effect on gamma-interferon production or natural killer cell activities.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 3093918 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1978 Jul;33(1):1-11. Related Articles, Links

A double-blind trial of transfer factor vs placebo in multiple sclerosis patients.

Collins RC, Espinoza LR, Plank CR, Ebers GC, Rosenberg RA, Zabriskie JB.

A double-blind trial of the effect of transfer factor on multiple sclerosis patients was carried out. In a series of fifty-six multiple sclerosis patients treated with monthly injections of either transfer factor or placebo for 1 year, no beneficial effect of transfer factor was noted. In addition, none of the immunological and serological parameters studied (measles migration inhibition, measles HI titre or CSF immunoglobulin) changed as a result of transfer factor therapy. Histocompatibility typing and CSF IgG/TP ratios were correlated with the disease activity. Of interest was the finding that the presence of the DW2 antigen, when unassociated with HLA-B7 antigen, appeared to correlate with the mildest form of disease activity.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 361313 [PubMed - indexed for MEDLINE]
Lancet. 1976 May 8;1(7967):988-90. Related Articles, Links

Transfer-factor therapy in multiple sclerosis.

Behan PO, Durward WF, Melville ID, McGeorge AP, Behan WM.

The effect of transfer factor prepared from relatives of patients with multiple sclerosis (M.S.) and from unrelated donors on the clinical course of M.S. has been studied in fifteen male and fifteen female patients. Some patients were given transfer factor and some placebo (physiological saline). Results of three independent clinical examinations by different neurologists and subjective assessments by the patients showed no difference between those given transfer factor and those given placebo.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 57441 [PubMed - indexed for MEDLINE]
Ann Neurol. 1983 Sep;14(3):333-8. Related Articles, Links

Natural killer cell activity in patients with multiple sclerosis given alpha interferon.

Rice GP, Casali P, Merigan TC, Oldstone MB.

The purpose of this study was to examine the function and regulation of natural killer cells in vitro and in vivo in patients with multiple sclerosis. Of 12 patients who received 5 X 10(6) international units of human alpha interferon, 9 demonstrated an increase in natural killer cell activity within 48 hours as defined by the lysis of 51Cr-labeled K-562 cells. The activity was normal before treatment, unlike that of tumor-bearing patients, and reached baseline levels within one week despite continuous interferon administration over the next six months. The same patients given a placebo preparation failed to show this enhanced natural killer cell activity. We also studied K-562 killing in 36 other patients and age- and sex-matched control subjects and were unable to demonstrate any differences between the two groups or any correlation of natural killer cell function with disease activity. The in vitro augmentation of natural killer cell activity by purified measles virions, which is associated with the release of interferon, and by the isolated glycoproteins of measles virus, which activates natural killer cells without the extracellular release of interferon, was similar in both patients and control subjects. Further, the proportion of cells defined by the monoclonal antibody HNK-1, which defines both natural killer cells and a small subset of cytotoxic T lymphocytes, was normal. In patients with multiple sclerosis, the normality of natural killer cell function, as defined by these several interrelated assays, speaks against a defect in this nonspecific antiviral defense mechanism in the pathogenesis of the disease.
Clin Exp Immunol. 1981 Mar;43(3):557-64. Related Articles, Links

A clinical and immunological study of the effects of transfer factor on multiple sclerosis patients.

Lamoureux G, Cosgrove J, Duquette P, Lapierre Y, Jolicoeur R, Vanderland F.

A clinical and laboratory trial was designated to test the value of a potentially active pool of transfer factor (TF) given for a period of 3 months, at weekly intervals, in 27 relapsing MS patients and controls. The pool of TF was extracted from peripheral lymphocytes of 36 normal individuals presensitized with DNCB as marker. It was biologically capable of transferring DNCB sensitivity to MS recipients and did not show any toxicity. Clinically, a slight but not significant improvement of the functional and disability indices was observed in the TF group over a period of 1 year, while both indices increased in the control group. The treatment had no influence on the number of relapses and/or on sensory and visually evoked potentials, axial tomography and electronystagmography. In laboratory tests, a significant difference was found in the total CSF protein (P less than 0 . 05) and IgG (P less than 0 . 01) levels in the two groups studied; both values decreased or were stabilized in the group receiving TF, while they increased in the control group. Whether or not these slight clinically and biologically beneficial effects were due to the high dose of TF given or to its biological activity remains to be established. This pilot study suggests that a more appropriate answer regarding TF in MS might be obtained by using biologically active material, given for longer periods of time, at a closer interval and in a larger number of patients.

Publication Types:
• Clinical Trial
• Randomized Controlled Trial

PMID: 7026094 [PubMed - indexed for MEDLINE]

1: S Afr Med J. 1976 Sep 18;50(40):1556-8.
Related Articles, Links

The use of transfer factors in the treatment of multiple sclerosis: a case report.

Sacks N, Potgieter HJ, Van Rensburg AJ.

A 23-year-old woman suffering from multiple sclerosis (MS) was given a course of 6 injections (0.5 U) of mumps transfer factor (TF) at 2-weekly intervals. The patient's symptoms improved dramatically and during the 10 months since treatment was instituted, no exacerbations have occurred. The possible aetiological role of paramyxoviruses in MS and the use of TF in the treatment of the disease are discussed. MS is however, a disease of exacerbations and spontaneous remissions, and despite our promising findings in this patient we wish to refrain from hailing mumps TF as a possible cure for this notorious disease.

Publication Types:
• Case Reports

PMID: 982209 [PubMed - indexed for MEDLINE]
Scand J Immunol. 1976;5(1-2):141-8. Related Articles, Links

Transfer factor treatment of patients with multuple sclerosis. I. Preliminary report of changes in immunological parameters.

Jersild C, Platz P, Thomsen M, Dupont B, Svejgaard A, Ciongoli AK, Fog T, Grob P.

In five patients with definite multiple sclerosis and lack of cell-mediated immunity to measles and parainfluenza virus antigens, various immunological parameters were studied before and during transfer factor treatment. The study showed that cell-mediated immunity to measles virus antigen, as evaluated by the leukocyte migration agarose test, could temporarily be restored, using repeated injections of transfer factor pooled from unselected, normal blood donors.

PMID: 178047 [PubMed - indexed for MEDLINE]

Letter: Transfer factor in multiple sclerosis.
Lancet. 1976 Jul 10;2(7976):99-100. No abstract available.
PMID: 59180 [PubMed - indexed for MEDLINE]

Schweiz Med Wochenschr. 1977 Dec 3;107(48):1742-3. Related Articles, Links

[Transfer factor therapy in a patient with anergic pulmonary tuberculosis]

[Article in German]

Kind CH, Gartmann JC, Grob PJ.

Report on a patient suffering from severe, relapsing pulmonary tuberculosis showing progressive clinical deterioration accompanied by the appearance of cutaneous anergy to tuberculin. In addition, the sputum cultures showed growth of Mycobacterium intracellulare. During therapy with transferfactorZurich there was a slow but impressive clinical improvement, the skin reactivity to tuberculin was reconstitued and the sputum cultures became negative. The radiological findings remained unchanged.

Publication Types:
• Case Reports

PMID: 929133 [PubMed - indexed for MEDLINE]
Schweiz Med Wochenschr. 1977 Dec 3;107(48):1742-3. Related Articles, Links

[Transfer factor therapy in a patient with anergic pulmonary tuberculosis]

[Article in German]

Kind CH, Gartmann JC, Grob PJ.

Report on a patient suffering from severe, relapsing pulmonary tuberculosis showing progressive clinical deterioration accompanied by the appearance of cutaneous anergy to tuberculin. In addition, the sputum cultures showed growth of Mycobacterium intracellulare. During therapy with transferfactorZurich there was a slow but impressive clinical improvement, the skin reactivity to tuberculin was reconstitued and the sputum cultures became negative. The radiological findings remained unchanged.

Publication Types:
• Case Reports

PMID: 929133 [PubMed - indexed for MEDLINE]
Med Clin (Barc). 1980 May 25;74(10):403-7. Related Articles, Links

[Cell immunity responses in patients with widespread neoplasias following administration of transfer factor (author's transl)]

[Article in Spanish]

Simo-Camps E, Vich JM, Garcia Calderon PA, Bofill D, Grau A, Anguiz A, Forcadell I.

PMID: 6968012 [PubMed - indexed for MEDLINE]
Ann Med Interne (Paris). 1979;130(11):517-21. Related Articles, Links

[Effect of transfer factor on the immunity state of patients with bronchopulmonary cancer. A report on 12 cases (author's transl)]

[Article in French]

Hainaut J, Challan-Belval P, Haguenauer G, Pellegrin J, Allard P, Kermarec J.

The dialysate of an extract of leucocytes having transfer factor (TF) activity was administered, at a daily dose of 1 mg/ml of orcinol-sulphuric positive material, by intramuscular injection to 12 patients with bronchopulmonary cancer for 6 days. An increase in the percentage of E-rosettes and the absolute number of T lymphocytes was observed in 7 cases out of 10. Rapid healing of a widespread intercurrent zona and a regin of B.C.G. scarification reaction was also noted. The TF was well tolerated in most cases.

PMID: 317697 [PubMed - indexed for MEDLINE]
Jpn J Surg. 1983 Jul;13(4):304-11. Related Articles, Links

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

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.

PMID: 6606065 [PubMed - indexed for MEDLINE]
Laryngoscope. 1978 Jan;88(1 Pt 2 Suppl 8):79-82. Related Articles, Links

Transference of cell mediated immunity in patients with head and neck cancer.

Vetto RM, Burger DR.

A group of 67 patients with head and neck cancer has been studied of which 40 have received immunologic transfer factor from a normal donor pool. Examination of these patients revealed that lymphocyte reactivity to nonspecific mitogrens is depressed in patients who have head and neck cancer to a much greater extent than is seen in patients with other types of tumors. Furthermore, the depression is more prevalent among patients who have been treated with radiation. Patients in the head and neck group who have received transfer factor show an initial decreased response to PHA stimulation in culture. This is not seen in a control group of head and neck cancer patients or in patients with nonsquamous cander. Thymus-derived lymphocytes are depressed in patients with head and neck cancer, irrespective of whether they have received radiation. Th T-lymphocyte levels increased in eight of 38 patients who received nonimmune transfer factor, but 7 of these were in the group who had not received radiation. The leukocyte adherence inhibition (LAI) test has been used to determine tumor immunity in the patient test group. Changes in tumor immunity did not occur in those patients who received normal nonimmune transfer factor. Studies are presently in progress which provide for treatment of patients with head and neck cancer with specific squamous carcinoma immune transfer factor.

PMID: 304143 [PubMed - indexed for MEDLINE]
Cell Immunol. 1983 Nov;82(1):147-62. Related Articles, Links

Cell-mediated immunity: correlation of mixed-leucocyte-macrophage migration inhibition with delayed-type hypersensitivity after immunization and donor-specific transfer of cell migration inhibition by dialyzable leucocyte extract.

Mazaheri R, Hamblin AS, Zuckerman AJ.

Active and adoptive sensitization of rhesus monkeys (Macacca mulatta) as well as the development of a novel sensitive in vitro cell migration inhibition assay for cell-mediated immunity (CMI) in this species are described. First, the correlation of mixed leucocyte-macrophage migration tests (LMMI) with the whole blood lymphocyte transformation (LT) and the delayed hypersensitivity skin test (DH) in immunized animals are shown. Second, these tests are used to demonstrate adoptive transfer of specific/nonspecific cellular immunity (CMI) with dialyzable leucocyte extract (DLE) from immunized donor to unimmunized recipient monkeys. Seventeen animals were immunized with keyhole limpet haemocyanin (KLH) or hepatitis B surface antigen (HBsAg) in Freund's complete adjuvant (FCA) or with FCA alone. Acquisition of antigen-specific cell-mediated immunity was detected by all three tests within 5 weeks of immunization. Positive LMMI responses were associated with positive DH and LT. However, there was no correlation between the magnitude or time of development of the three responses. Therefore, the LMMI test, like the LT test, is an in vitro parameter of DH, but reflects the activity of different subpopulations of lymphocytes and is regulated by different mechanisms. In addition, 12 naive animals received DLE. Within 3 weeks, transfer of sensitivity was detected towards antigens to which the recipients had previously not been reactive but the donors had been. An enhancement of transformation response to phytohaemagglutinin was also seen. Thus, rhesus DLE contains both donor-specific transfer factor-like and nonspecific adjuvant-like activities. In DLE recipients, unlike immunized animals, LMMI responses were dissociated from DH or LT responses in that positive LMMI was mostly seen with negative DH or LT to antigens. Therefore, LMMI emerged as the most sensitive assay for detecting adoptive transfer of CMI by DLE in vivo, supporting the view that different mechanisms regulate LMMI, LT, and DH.

PMID: 6196129 [PubMed - indexed for MEDLINE]
Med Vet Mycol. 1990;28(1):35-46. Related Articles, Links

Transfer of cell-mediated immunity to Paracoccidioides brasiliensis in hamsters with dialysable leukocyte extracts.

Peracoli MT, Montenegro MR, Soares AM, Mota NG.

Department of Microbiology and Immunology, Institute of Biological Sciences-UNESP, Brazil.

Dialysable leukocyte extracts (DLE) were obtained from lymph nodes and spleen cells of hamsters immunized with Paracoccidioides brasiliensis (immune DLE) or from non-immunized hamsters (non-immune DLE). Sensitivity to P. brasiliensis antigen (PbAg) was transferred by immune DLE to normal recipient hamsters and could be detected by the macrophage migration inhibition (MIF) assay on day three and by a positive skin test to PbAg on day seven after DLE inoculation. This reactivity persisted for 120 days. The specificity of DLE was studied by inoculation of immune or non-immune DLE into normal hamsters and transfer was evaluated 7 days later by the MIF assay and by skin tests to PbAg, Candida albicans antigen (CaAg), sonically treated bacille Calmette-Guerin (BCG) (SBCG) and ovalbumin (OVA). The immune DLE recipients showed a reactivity to PbAg that was significantly stronger than that of the nonimmune DLE recipients although both groups of recipient animals showed reactivity to CaAg and SBCG. The results suggest that both DLE preparations contain a non-specific antigen augmenting factor. This factor may stimulate the minimal background response to the antigens in nonimmunized recipient hamsters.

PMID: 1694543 [PubMed - indexed for MEDLINE]
Mycopathologia. 1993 Mar;121(3):149-56. Related Articles, Links

Dialysable leukocyte extracts modify the course of experimental paracoccidioidomycosis in the Syrian hamster.

Peracoli MT, Rezkallah-Iwasso MT, Mota NG, Montenegro MR.

Department of Microbiology, School of Medicine, UNESP, Botucatu, Brazil.

The effect of dialysable leukocyte extracts (DLE) obtained from hamsters immunized with Paracoccidioides brasiliensis (immune DLE) and from non-immunized hamsters (non-immune DLE) was studied in hamsters inoculated with P. brasiliensis by the intratesticular route. Treatment with immune or non-immune DLE was started during the third week of infection and was repeated at 7, 11, 15 and 19 weeks. A group of untreated infected animals was used as control. Animals were submitted to the delayed hypersensitivity skin test to P. brasiliensis antigen (PbAg) in vivo and assayed in vitro by the macrophage migration inhibition test in the presence of Phytohemagglutinin (PHA) and PbAg and by immunodiffusion for specific antibody. The animals were sacrificed at 4, 8, 12, 16 and 20 weeks. The morphology and extension of the lesions were studied at the inoculation site, and in lymph nodes, lungs, liver, spleen and kidneys. In contrast to the controls, animals treated with both DLEs maintained a positive cell-mediated immune response throughout the experiment and developed less extensive infection with a significantly lower number of fungi in the lesions. The results suggest that immune and non-immune DLE preparations modified the evolution of experimental paracoccidioidomycosis with equal efficiency. This similarity may be explained by the immunoregulatory activities of both extracts.

PMID: 8474531 [PubMed - indexed for MEDLINE]

Dialysable leukocyte extracts (DLE) may induce marked changes in the immune expression of human recipients. It is unclear whether the conversion of skin reactivity by DLE is due to a donor-related specific transfer factor or to an antigen nonspecific augmenting factor which enhances a preexisting low-level response in DLE recipients. In this study, DLE from immunized and unimmunized human and calf donors or saline was administered to 88 medical students. The recipient population demonstrated minimal background responses to the test antigens keyhole limpet haemocyanin (KLH) and horseshoe crab haemocyanin (HCH). The results indicate that the DLE preparations from both immunized and unimmunized donors significantly stimulated skin reactivity but not in vitro responses to both KLH and HCH in the recipient population. The results suggest that these DLE preparations contain an immunologically nonspecific augmentor, which stimulates a preexisting low-level response in the unimmunized population
Poult Sci. 1984 Jul;63(7):1333-7. Related Articles, Links

Adoptive transfer of delayed hypersensitivity and protective immunity to Eimeria tenella with chicken-derived transfer factor.

Klesius PH, Giambrone JJ.

Delayed hypersensitivity (DH) and protective immunity were transferred to nonimmune 4- and 10-week-old broiler chickens with transfer factor (TF) prepared from splenic leukocytes of chickens immunized with CocciVac D. Only chickens injected with the immune TF showed DH by wattle reaction to oocyst antigen and protective immunity to Eimeria tenella challenge infection. Chickens given a single injection of TF 5 days before challenge infection exhibited a significant (P less than .05) DH response at the time of infection. Immune TF preparations were active at concentrations of 100, 200, or 400 mg. Neither DH nor protective immunity was transferred to chickens injected with the TF-diluent control or nonimmune TF. The nonimmune TF was prepared from chickens kept free of coccidial infection. These findings indicated that TF prophylaxis produced beneficial results in nonimmune chickens by conferring some protection against challenge with E. tenella. The effects of TF on T-lymphocyte mediated protective immunity to coccidia in chickens are discussed.

PMID: 6473247 [PubMed - indexed for MEDLINE]
to become a clearly observable skin reaction.
Clin Immunol Immunopathol. 1987 Mar;42(3):360-9. Related Articles, Links

An animal model for evaluation of antigen-specific dialyzable leukocyte extracts therapy of osteosarcoma.

Tsang KY, Pan JF, Fudenberg HH.

The effects of human osteosarcoma (OS)-specific dialyzable leukocyte extracts (DLE) in hamsters bearing human OS were investigated. The DLE used in this investigation was prepared from rabbits immunized with human osteosarcoma-associated antigens (DLE-OSAA). Tuberculin (DLE-PPD) and control DLE were prepared from rabbits injected with tuberculin or 0.85% NaCl (DLE-NaCl). DLE was administered subcutaneously into inbred hamsters (each injection contained DLE derived from 10(7) rabbit leukocytes). Four groups of animals were studied: group 1, amputation alone; group 2, amputation plus DLE-OSAA; group 3, amputation plus DLE-PPD; group 4, amputation plus DLE-NaCl. Of the DLE-OSAA-treated animals (group 2), 60% were still alive at 300 days postamputation; whereas in animals in groups 1, 3,

and 4, all died within 90 days postamputation. In separate experiments, we found that 100% of the animals in groups 1, 3, and 4 developed pulmonary metastases within 30-60 days postamputation, whereas only 20% of the animals in group 2 developed metastases at the same time; indeed 40% of the DLE-OSAA-treated animals were free of metastases in 240-300 days postamputation. Both the leukocyte adherence inhibition assay (LAI) and lymphocyte DNA synthesis assay (LDS) were used to monitor the transfer of antigen-specific cell-mediated immunity in each group of tumor-bearing hamsters. All surviving hamsters in group 2 had high LAI and LDS activity. Our results suggest that DLE-OSAA is effective in preventing pulmonary metastases and death of OS-bearing hamsters (after amputation) as compared with amputation alone, amputation plus DLE-NaCl, and amputation plus DLE-PPD, and that its effect is via an antigen-specific mechanism.

PMID: 3470162 [PubMed - indexed for MEDLINE]
Allergol Immunopathol (Madr). 1990 Sep-Oct;18(5):269-75. Related Articles, Links

Mitigating effects of dialysable leukocyte extract (DLE) on the experimental allergic uveitis (EAU) of the rabbit.

Fricke HJ, Schroder KD, Metzner G, Schroder I, Haroske D, Tilgner S, Sych FJ, Klein S, Jager L.

Department of Ophthalmology, Friedrich Schiller University, Jena, Federal Republic of Germany.

Experimental allergic uveitis (EAU) is an induced autoimmune disease by administering soluble retinal S antigen and complete Freund's adjuvant (CFA). In rabbits, the result is the occurrence of chorioretinitis in 90% of the cases. The first inflammation is followed by spontaneous relapses. The EAU of the rabbit was utilized to study the effects of the dialyzable leucocyte extract (DLE) on the course and the intensity of the disease in this autoimmune model. The DLE preparations examined differed with regard to their origin or the immunological stimulation of the initial material (DLE from humans (DLE Hu) and DLE from the normal rabbit (DLE RaO) or rabbits which had EAU (DLE RaEAU) and rabbits which had received CFA (DLE Ra (CFA). One unit of DLE corresponds to the extract from 10(9) cells. The administration of DLE starts with the onset of inflammation. 4 x 0.5 units were administered during the first week, 1 x 0.5 units per week from the 2nd to the 12th week. All preparations decrease the cumulative frequency of the days of illness significantly. The duration of the initial inflammation is reduced in all animals treated, but only in part significantly. There appears a graduation of efficacy: DLE RaEAU greater than DLE Ra CFA greater than DLE Hu greater than DLE RaO. Overall, it can be seen that, on the one hand, there is no specificity or restriction of the species for the efficacy and, on the other hand, the extent of the effects depends on the degree of the immunological stimulation. The maximum efficacy of DLE RaEAU is not exclusively due to the transmission of an antigen-specific sensitization.(ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 2097893 [PubMed - indexed for MEDLINE]
Z Gesamte Inn Med. 1989 Nov 15;44(22):684-7. Related Articles, Links

[The effect of long-term dialysable leukocyte extract therapy on the recurrence behavior of idiopathic uveitis]

[Article in German]

Fricke HJ, Fricke B, Metzner G, Haroske D.

Klinik fur Innere Medizin des Bereiches Medizin der Friedrich-Schiller-Universitat Jena.

26 patients with idiopathic uveitis (anterior uveitis 11, intermediate uveitis 8, posterior uveitis 7) were treated with Dialysable Leukocyte Extract (DLE) for a long period. In comparison with the period before DLE in anterior and posterior uveitis the numbers of relapses decrease, the inflammation-free intervals become longer. These prolongations are significant. In cases with intermediate uveitis such a significance is not available. But in all types of uveitis DLE therapy shortens the duration of inflammatory episodes. These effects lead to a highly significant decrease of the portion of the period during and after DLE therapy in which inflammatory signs occur in comparison with the period before DLE therapy. The latter result becomes evident for all types of uveitis.

PMID: 2626848 [PubMed - indexed for MEDLINE]
Arch Immunol Ther Exp (Warsz). 1994;42(4):295-9. Related Articles, Links

Influence of various forms of dialyzable leukocyte extracts on rat adjuvant arthritis.

Stancikova M, Rovensky J, Pekarek J, Orvisky E, Blazickova S, Cech K.

Research Institute of Rheumatic Diseases, Slovak Republic.

Adjuvant-induced arthritis in rats is a chronic inflammatory disease, widely used as an animal model for rheumatoid arthritis. In our study the effect of various fractions of dialyzable leukocyte extract (DLE): DLE I-molecular weight below 10 kDa (commercial preparation), DLE II-molecular weight below 5 kDa (suppressor fraction), DLE III-molecular weight 5-10 kDa on rat adjuvant-induced arthritis was studied. The adjuvant arthritic (AA) rats were treated with DLE fractions i.p. in solutions containing an active substance isolated from 12.5 x 10(6) and 6.25 x 10(6) leukocytes from day 1 (adjuvant injected) through day 18, every second day (total 9 times). Various markers of inflammation, immune function and joint destruction were evaluated: hindpaw volume, serum hyaluronic acid, serum albumin and biopterin in urine. All these markers showed a significant improvement after using fraction DLE II in comparison with AA controls. Fractions DLE I and DLE III influenced only some markers of inflammation and immune function. Our results demonstrated a therapeutical effect of fraction DLE II on rat adjuvant-induced arthritis.

PMID: 7487370 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):33-40. Related Articles, Links

Inhibition of in vitro HIV infection by dialysable leucocyte extracts.

Fernandez-Ortega C, Dubed M, Ruibal O, Vilarrubia OL, Menendez de San Pedro JC, Navea L, Ojeda M, Arana MJ.

Department of Cellular Biology, Center for Biological Research and Center for Genetic Engineering and Biotechnology, Havana, Cuba.

Dialysable Leucocyte Extract (DLE) is a low molecular weight dialysable material of disrupted peripheral human leucocytes with widespread effects on the immune system. We described the in vitro anti-HIV activity of DLE as well as its three chromatographic fractions (Fa, Fb and Fc). To determine the levels of inhibition on HIV replication by DLE we infected MT-4 cell cultures, using the Bru viral isolate at 0.05, 0.1, 0.5 and 1 m.o.i. Previously, MT-4 cells cultures were treated with DLE or fractions at non-toxic concentrations. Reverse transcriptase (RT) activity and p24 antigen were evaluated in culture supernatants at seven days postinfection. No effect was observed when MT-4 cells were incubated with DLE for 3 h. Whereas inhibition of HIV production was observed when MT-4 cells were pre-treated for a longer period of time. DLE inhibited p24 production and RT activity more than 50% at 0.1 m.o.i. More than 80% of inhibition was observed for all doses of DLE tested at 0.05 m.o.i. Higher viral doses (m.o.i. 0.5 and 1) were used to assess the antiviral activity of DLE fractions. Fraction Fb inhibits viral production more than 80%. Otherwise, fractions Fa and Fc did not show inhibitory effect for any viral dose used. These results indicate that DLE is able to modulate cell susceptibility to viral infection in vitro.

PMID: 8993755 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):163-70. Related Articles, Links

Dialysable leucocyte extract (DLE) reduces lipopolysaccharide-induced tumour necrosis factor secretion in human leucocytes.

Ojeda Ojeda M, Fernandez Ortega CB, Arana Rosainz MJ.

Department of Cell Biology, Center for Biological Research, Havana, Cuba.

Dialysable leucocyte extract (DLE), obtained from lysed leucocytes, provide clinical effectiveness in a broad spectrum of diseases. Tumour necrosis factor (TNF) is raised in AIDS patients leading to an increase in human immunodeficiency virus (HIV) replication in vitro [1,2], whereas progression to AIDS in asymptomatic HIV infected individuals is retarded under treatment with DLE. In the present study we tested the DLE effect in vitro on both TNF biological activity (cytotoxicity) in L929 cells and its induction by lipopolysaccharide (LPS) in human monocytes as well as in whole blood from healthy donors. When monocytic cells were simultaneously exposed to LPS and DLE during a period of 5 1/2 hours, the induction of TNF was strongly diminished. The same inhibitory effect of DLE on TNF induction was observed when LPS was added to the culture medium prior to DLE. No significant effect of DLE on TNF-mediated cytotoxicity, even in the presence of the highest concentrations of DLE tested, was detected. DLE treatment of whole human blood regulates responses to LPS: simultaneous in vitro exposure to endotoxin provokes a remarkable decrease (4- and 1.6-fold) of TNF release. In pre-incubation experiments, TNF production was largely reduced or completed abrogated. These results could, in part, explain the in vivo observed effect, when under treatment with this extract, the progression to AIDS of HIV-infected individuals was retarded. The results suggest that "natural' substances like DLE may be important immunomodulators in inflammatory diseases.

PMID: 8993776 [PubMed - indexed for MEDLINE]
Int J Immunopharmacol. 1997 Aug;19(8):431-6. Related Articles, Links

Stimulation of hemopoietic colony formation from mouse marrow cells in vitro using human dialyzable leukocyte extracts-IMMODIN-SEVAC.

Vacek A, Barnet K, Hofer M, Cech K, Pekarek J, Schneiderova H.

SEVAC a.s. Prague, Czech Republic.

The influence of dialyzable extract from human leukocytes (DLE) on the in vitro growth of the granulocyte-macrophage colony-forming cell (GM-CFC) colonies from progenitors of mouse bone marrow cells was studied. DLE alone did not induce the colony growth but it modulated the number of colonies if administered together with a colony-stimulating factor (CSF). The costimulatory effect prevailed in a broad range of DLE dilution and the index of increase was enhanced with the lowering of the CSF concentration. The costimulatory augmentation of clonal proliferation of GM-CFC with DLE was further strengthened by addition of indomethacin, thus indicating an intervening role of prostaglandins in the modulatory influence of DLE.

PMID: 9568548 [PubMed - indexed for MEDLINE]
Int J Immunopharmacol. 2000 Aug;22(8):623-34. Related Articles, Links

Positive effects of dialyzable leukocyte extract (DLE) on recovery of mouse haemopoiesis suppressed by ionizing radiation and on proliferation of haemopoietic progenitor cells in vitro.

Vacek A, Hofer M, Barnet K, Cech K, Pekarek J, Schneiderova H.

Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno, Czech Republic.

Dialyzed leukocyte extract (DLE) (Immodin SEVAC, Czech Republic) was shown to enhance the recovery of the pools of hemopoietic stem cells (CFUs) and of granulocyte-macrophage hemopoietic progenitor cells (GM-CFC) in the bone marrow in vivo, as well as to increase the numbers of leukocytes and thrombocytes in the peripheral blood of mice exposed to a sublethal dose of gamma-rays, with an ensuing increase in the numbers of mice surviving the lethal radiation dose. In experiments performed in vitro, DLE or sera of mice administered with DLE were added to cultures of intact mouse bone marrow cells containing suboptimal concentrations of hemopoietic stimulatory cytokines, namely recombinant mouse interleukin-3 (rmIL-3) or recombinant mouse granulocyte-macrophage colony-stimulating factor (rmGM-CSF); under these experimental conditions, both DLE and sera of mice administered DLE were found to increase the counts of GM-CFC colonies in the cultures. It can be hypothesized on the basis of the findings obtained in vitro that the described co-stimulating activity (CoSA) of DLE may play a role also under in vivo conditions; the enhancement of the recovery of hemopoiesis suppressed by ionizing radiation may be due to a co-operation of the stimulatory effects of DLE with the action of cytokines endogenously produced in irradiated tissues.

PMID: 10988357 [PubMed - indexed for MEDLINE]
Immunopharmacol Immunotoxicol. 2002 Nov;24(4):651-64. Related Articles, Links

Hemopoiesis-stimulating effects and enhanced survival of irradiated mice after peroral or intraperitoneal administration of ultrafiltered pig leukocyte extract (UPLE, IMUNOR).

Vacek A, Hofer M, Hromas J, Luksikova E, Svoboda J, Schneiderova H.

Institute of Biophysics, Academy of Sciences of the Czech Republic, Kralovopolska 135, CZ-612 65 Brno, Czech Republic. vacek@ibp.cz

Ultrafiltered pig leukocyte extract (UPLE, IMUNOR, ImunomedicA, Usti nad Labem, Czech Republic) administered perorally (p.o.) or intraperitoneally (i.p.) enhanced recovery of the pool of granulocyte-macrophage hemopoietic progenitor cells (GM-CFC) in the bone marrow of normal or sublethally irradiated mice and increased survival of mice exposed to a lethal radiation dose. In experiments in vitro, sera of mice treated with UPLE p.o. or i.p. induced GM-CFC colony formation in cultures of normal mouse bone marrow cells, i.e., produced colony-stimulating activity (CSA). UPLE alone did not induce GM-CFC colony growth, i.e., had no CSA. When UPLE alone or sera of mice administered UPLE p.o. or i.p. were added to bone marrow cultures containing suboptimal concentration of recombinant mouse interleukin-3 (rmIL-3), both UPLE and the sera increased the counts of GM-CFC colonies in comparison with cultures containing only rmIL-3, i.e., produced co-stimulating activity (CoSA). Based on the findings obtained in vitro, it can be hypothesized that the described CSA and CoSA of UPLE may play a role also under in vivo conditions; enhancement of the recovery of hemopoiesis suppressed by ionizing radiation may be due to co-operation of the stimulatory effects of UPLE with the action of cytokines endogenously produced in irradiated tissues.

PMID: 12510796 [PubMed - indexed for MEDLINE]
Decreased production of cytokines after cytomegalovirus infection of marrow-derived stromal cells.

Lagneaux L, Delforge A, Snoeck R, Stryckmans P, Bron D.

Service de Medecine Interne, Institut J. Bordet, Brussels, Belgium.

Cytomegalovirus (CMV) infection is frequently associated with graft failure in bone marrow transplant patients; the pathogenesis of this myelosuppression in not clearly understood. We have previously documented that CMV-induced myelosuppression is related to an alteration of the marrow microenvironment. To further investigate the effect of CMV on stromal cell function, conditioned media (CM) from CMV-infected or uninfected stromal cells were tested for their capacity to promote the growth of granulocyte/macrophage colony-forming cells (CFU-GM) and for their concentration in colony-stimulating factors (CSFs) such as interleukin-3 (IL-3), IL-6, granulocyte-macrophage and granulocyte colony-stimulating factors (GM-CSF and G-CSF). CM from CMV-infected stromal cells failed to sustain granulocyte-macrophage colony-forming unit (CFU-GM) growth. The production of IL-6, GM-CSF, and G-CSF, measured by enzyme-linked immunosorbent assay (ELISA), was 21,150 +/- 3392, 57 +/- 15, and 2340 +/- 717 pg/mL, respectively, in CMV-infected stromal cells stimulated by lipopolysaccharide (LPS) and was significantly decreased ($p < 0.01$) from the control values (177,138 +/- 98,692, 113 +/- 20, and 5533 +/- 1306 pg/mL). These results suggest that the myelosuppressive effect of CMV is primarily due to a lack of CSF production. To further document this hypothesis, primitive marrow progenitor cells (blast colony-forming cells [Bl-CFC]) cultured on CMV-infected stromal layer have been grown in the presence of IL-3 (20 ng/mL), IL-6 (20 ng/mL), GM-CSF (40 ng/mL), and G-CSF (50 ng/mL). Used alone, all these CSFs partially reverse the CMV-induced inhibition of Bl-CFC growth; the combination of these CSFs completely restores normal Bl-CFC values. These data strongly suggest that CMV-induced myelosuppression is related to the lack of CSF production by the cells of the marrow microenvironment.

PMID: 7506672 [PubMed - indexed for MEDLINE]
1: Nouv Presse Med. 1978 Sep 23;7(32):2866-7.
Related Articles, Links

[Herpes keratites treated by leukocyte extracts dialysates (author's transl)]

[Article in French]

Hainaut J, Vignat JP, Saint-Blancard J, Fabre G, Sarrouy J, Allary M.

Publication Types:
• Case Reports
• Letter

PMID: 714668 [PubMed - indexed for MEDLINE]
1: Proc Virchow Pirquet Med Soc. 1980 Dec;34:3-87.
Related Articles, Links

Immunotherapy with dialyzable leukocyte extracts and studies of their antigen-specific (transfer factor) activity.

Fudenberg HH, Wilson GB, Smith CL.

Publication Types:
• Review

PMID: 6270691 [PubMed - indexed for MEDLINE]
Adv Exp Med Biol. 1981;137:293-323. Related Articles, Links

Modulation of cell-mediated responses with dialyzable leukocyte extract containing transfer factor.

Klesius PH.

Publication Types:
• Review

PMID: 6174037 [PubMed - indexed for MEDLINE]

Comp Immunol Microbiol Infect Dis. 1980;3(3):247-60. Related Articles, Links

Comparative studies on dialyzable leukocyte extracts containing transfer factor--a review.

Klesius PH, Fudenberg HH, Smith CL.

Publication Types:
• Review

PMID: 6162606 [PubMed - indexed for MEDLINE]
Postepy Hig Med Dosw. 1981 Nov-Dec;35(6):549-74. Related Articles, Links

[Transfer factor (TF) - a modulator of immunological activity]

[Article in Polish]

Grubek-Jaworska H, Komorowska-Rycerz A.

Publication Types:
• Review

PMID: 6752921 [PubMed - indexed for MEDLINE]
Cancer Treat Rev. 1979 Dec;6(4):209-15. Related Articles, Links

Transfer factor.

Al-Sarraf M, Baker LH.

Publication Types:
• Review

PMID: 394838 [PubMed - indexed for MEDLINE]
Med Clin North Am. 1976 May;60(3):585-90. Related Articles, Links

Transfer factor: a potential agent for cancer therapy.

LoBuglio AF, Neidhart JA.

This review has attempted to describe the characteristics of transfer factor which make it a very attractive potential agent for immunotherapy. Preliminary observations suggest that it may be capable of modifying resistance to a variety of diseases including cancer but considerable progress in basic knowledge regarding this agent is crucial to its successful application in clinical disease states. Fortunately, a sizable number of interested and dedicated investigators are exploring these difficult problems and their success may lead to new approaches in immunotherapy.

Publication Types:
• Review

PMID: 775210 [PubMed - indexed for MEDLINE]
Cancer. 1976 Jan;37(1):90-7. Related Articles, Links

Transfer factor therapy in patients with cancer.

Vetto RM, Burger DR, Nolte JE, Vandenbark AA, Baker HW.

The objective of this study was to utilize transfer factor to stimulate cell-mediated immunity to specific tumor antigens in cancer patients. Thirty-five selected patients with advanced recurrent cancer, who were not suitable for further conventional therapy, were treated with transfer factor. Transfer factor was prepared from cohabitants of the patients and administered at 2-week intervals. This immunotherapeutic approach produced a clinical effect in 13 patients in terms of regression of tumor (1), arrest of metastatic disease (14), or pain relief (14). Conversion of dermal reactivity to specific

tumor antigens was observed during periods of clinical improvement. Despite continued immunotherapy, the duration of clinical improvement was short (2 weeks to 12 months). Seven of the 11 patients not responding to therapy exhibited serum blocking of lymphocyte responsiveness. In 11 patients there is insufficient data to evaluate the clinical effectiveness of this therapy. The results suggest that transfer factor can stimulate specific cell-mediated immunity in cancer patients and produce a clinical effect on tumor under certain circumstances.

PMID: 1247971 [PubMed - indexed for MEDLINE]
Acta Neurol Scand Suppl. 1977;63:227-37. Related Articles, Links

Immunotherapy in infectious disease, autoimmunity and cancer.

Spitler LE, Dau PC.

The clinical and immunologic effects of transfer factor and of levamisole were evaluated in over 200 patients with a variety of diseases. With transfer factor, the most encouraging results were observed in patients with the Wiscott-Aldrich syndrome, chronic mucocutaneous candidiasis, coccidioidomycosis, Behcet's disease and malignant melanoma. With levamisole, the most promising results were observed in patients with recurrent aphthous stomatitis, rheumatoid arthritis and herpes simplex infections, especially ocular herpes. Immunologically, transfer factor usually caused conversion of skin test reactivity and conversion of in vitro tests of cellular immunity as well, whereas levamisole caused increases in skin test reactivity without a parallel change in in vitro para meters, suggesting that the two agents may have different mechanisms of action. In a limited number of patients with multiple sclerosis, reactivity to three viral antigens was found to be lower than that in normal subjects, as measured by lymphocyte stimulation. Following levamisole therapy, this reactivity increased to normal levels, but the patients did not show clinical benefit.

PMID: 265668 [PubMed - indexed for MEDLINE]
J Surg Oncol. 1982 Sep;21(1):5-8. Related Articles, Links

A critical review of immunotherapy of disseminated renal adenocarcinoma.

Montie JE, Bukowski RM, James RE, Straffon RA, Stewart BH.

Sixty patients with renal adenocarcinoma have been treated with five different immunotherapy trials consisting of 1) Transfer Factor (TF), 2) TF and Bacillus Calmette-Guerin (BCG), 3) TF, BCG, Chloroethyl-cyclohexy-nitrosurea (CCNU) and megestrol acetate (Megase), 4) BCG, CCNU, and Megase, or 5) BCG. Using strict response criteria for measurable disease, objective responses were seen in 14-22% of cases. While this nonspecific immunotherapy of renal adenocarcinoma has been associated with documented regression of metastases, response rates are similar to that obtained with hormonal therapy alone. Objective responses support the concept of further trials in this disease with more sophisticated immunotherapy.

PMID: 7109637 [PubMed - indexed for MEDLINE]
Cancer Res. 1983 Feb;43(2):940-7. Related Articles, Links

Renal cell carcinoma: antitumor effects of leukocyte interferon.

Quesada JR, Swanson DA, Trindade A, Gutterman JU.

Partially purified human leukocyte (alpha) interferon was administered i.m. at a dose of 3 x 10(6) units/day to 19 patients with metastatic renal cell carcinoma. Five patients (26%) showed partial responses; two patients (10.5%), objective minor responses; three patients (16%), mixed effects (evidence of biological effect with regression of some lesions but concomitant progression); two patients (10.5%), disease stabilization; and seven patients (37%), progressive disease. All tumor responses were seen in lung or mediastinal metastases. Tumor response significantly correlated with interferon-induced leukopenia and granulocytopenia and with pretreatment performance status. Antibodies to interferon were found in one patient prior to treatment. We concluded that interferon is a potential active antitumor agent in patients with renal cell carcinoma.

Publication Types:
• Clinical Trial

PMID: 6336662 [PubMed - indexed for MEDLINE]
J Urol. 1999 Jul;162(1):43-5. Related Articles, Links

Interleukin-2 based immunotherapy for metastatic renal cell carcinoma with the kidney in place.

Wagner JR, Walther MM, Linehan WM, White DE, Rosenberg SA, Yang JC.

Urologic Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA.

PURPOSE: We assessed morbidity, response and survival in patients with metastatic renal carcinoma treated with high dose intravenous interleukin-2 (IL-2) based immunotherapy with the primary renal tumor in place. MATERIALS AND METHODS: We retrospectively analyzed the records of patients with metastatic renal carcinoma and the primary kidney tumor in situ who were treated at the surgery branch of the National Cancer Institute. Of the patients 607 were treated with IL-2 based therapy. Patient age, sex, sites of extrarenal disease, morbidity, and response and survival rates were examined. RESULTS: From 1986 to 1996, 51 patients with the majority of disease at extrarenal sites were treated with the primary tumor in place. Treatment involved IL-2 based regimens, reflecting the evolution of immunotherapy at the National Institutes of Health. When evaluating only extrarenal sites, response was complete in 1 and partial in 2 of the 51 cases (6%). No responses were noted in the primary renal tumor. Three patients with responses at extrarenal sites underwent nephrectomy. The duration of response in these 3 cases was greater than 88, 11 and 4 months, respectively. Median survival in all 51 patients was 13 months (range 1 to 86). CONCLUSIONS: Select patients may be treated with IL-2 based immunotherapy with the primary renal tumors in place with morbidity. A randomized study is needed to assess the role of cytoreductive nephrectomy for treating metastatic renal cell carcinoma.

PMID: 10379736 [PubMed - indexed for MEDLINE]
Br J Cancer. 1976 Jun;33(6):606-11. Related Articles, Links

In vitro production of a transfer factor specific for transitional-cell carcinoma of the bladder.

Pizza G, Viza D, Boucheix C, Corrado F.

Human dialysable Transfer Factor (TFd) extracted from lymphocytes of patients with transitional cell carcinoma of bladder (TCCB) was replicated in culture by lymphoblastoid cell lines. The effectiveness of two such TFdLs produced in vitro in transferring sensitivity to TCCB was assessed in the lymphocyte migration test (LMT) using formalin-treated TCCB cells as antigen. The results, showed that one TFdL transferred sensitivity in 5/14 cases and the other in 12/15, not only to leucocytes of healthy individuals but also to leucocytes of TCCB patients. Preliminary results showing an in vivo transfer of sensitivity are discussed.

PMID: 938610 [PubMed - indexed for MEDLINE]
Biotherapy. 1996;9(1-3):123-32. Related Articles, Links

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

Pizza G, De Vinci C, Cuzzocrea D, Menniti D, Aiello E, Maver P, Corrado G, Romagnoli P, Dragoni E, LoConte 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.

Publication Types:
• Clinical Trial

PMID: 8993770 [PubMed - indexed for MEDLINE]
: Arch Esp Urol. 1989;42 Suppl 2:191-6. Related Articles, Links

[Immunotherapy with transfer factor in hormone-resistant metastasized carcinoma of the prostate]

[Article in Spanish]

Corrado F, Pizza G, de Vinci C, Corrado G.

Fifty-six patients with metastatic hormone-resistant carcinoma of prostate (stage D3) were submitted to immunotherapy with a monthly intramuscular injection of predominantly specific transfer factor (TF) produced in vitro. Patient follow-up ranging from 1 to 8 years revealed completed remission was achieved in one patient, partial remission in 6, and there was no progression of the metastatic disease in 14 patients. The mean patient survival was 17 months, higher than the survival rates reported elsewhere. No negative side effects ascribable to the treatment regimen were observed. All the foregoing findings, particularly the absence of side effects, provide encouraging data on this treatment modality.

PMID: 2639623 [PubMed - indexed for MEDLINE]
Am J Reprod Immunol Microbiol. 1985 Jul;8(3):80-3. Related Articles, Links

Effect of transfer factor on tumor-associated immunity and tumor growth of the Dunning R-3327G rat prostate adenocarcinoma.

Shaw MW, Ablin RJ, Guinan PD, Bhatti RA.

Of importance in the design and application of improved or new modalities of treatment are their evaluation on relevant animal models. In the case of prostate cancer (PCa) the Dunning R-3327 rat prostate adenocarcinoma (PCa), and its variant sublines, is one such experimental tumor model of its human counterpart. In a preliminary study, the effect of transfer factor (TF), one form of passive immunotherapy, on tumor-associated immunity (TAI) and tumour growth and histology of the G subline (a poorly differentiated, fast-growing, androgen sensitive, and poorly metastatic tumour of the Dunning R-3327 rat PCa) has been evaluated. TF prepared from the leukocytes of tumor-bearing animals and nontumor-bearing animals referred to as sensitized (STF) and unsensitized (UTF), respectively, had no significant effect on TAI or tumor size. The only noticeable effect of TF in this study was the presence of variable and moderate lymphocytic infiltrates, necrosis, and degenerative-type cells in tumors of animal recipients of STF. The failure to observe significant differences in TAI among tumor bearing and nontumor bearing animals raises doubt in part, of the immunogenicity of the G subline tumor and its appropriateness, at least for subsequent immunological studies. Further factors considered in this regard, are questions of tumor load, including the possible need for the use of adjuvant, and the parameters and sensitivity of immune responsiveness selected for evaluation and immunocompetency. Subsequent evaluation of the effect of TF on other more immunogenic variant sublines of the Dunning R-3327 rat tumor may yet provide further and more useful information.

PMID: 4025670 [PubMed - indexed for MEDLINE]
Boll Soc Ital Biol Sper. 1987 Nov 30;63(11):1043-50. Related Articles, Links

[Effects of transfer factor on the number of circulating lymphocytes in patients with spinocellular carcinoma of the cervicofacial area]

[Article in Italian]

Mastromatteo V, Negri L, Pacchioni D, Calabrese F, Giacomasso S, Fazio M.

PMID: 3454189 [PubMed - indexed for MEDLINE]
Soc Ital Biol Sper. 1987 Nov 30;63(11):1051-8. Related Articles, Links

[Changes in circulating lymphocytes and "E" rosettes in patients with colonic neoplasms treated with transfer factor]

[Article in Italian]

Negri L, Pacchioni D, Calabrese F, Giacomasso S, Mastromatteo V, Fazio M.

PMID: 3331288 [PubMed - indexed for MEDLINE]
J Immunol. 1977 May;118(5):1672-6. Related Articles, Links

In vitro augmentation of lymphocyte sheep cell rosette formation by leukocyte dialysates.

Holzman RS, Lawrence HS.

We have studied in vitro the effects of leukocyte dialysates containing transfer factor on the formation of sheep cell rosettes by human lymphocytes. Dialysate had no effect on the toral rosettes, but increased the number of rapidly forming

("active") rosettes. This was due to an increased affinity of the lymphocytes for the sheep red cell. Trypsin-treated lymphocytes regained the ability to form rosettes more rapidly when cultured with leukocyte dialysates than with control media. These experiments suggest that leukocyte dialysate acts to increase the number or arrangement of sheep cell receptors on the lymphocyte surface.

PMID: 323356 [PubMed - indexed for MEDLINE]
Acta Med Acad Sci Hung. 1980;37(1):83-8. Related Articles, Links

The effect of transfer factor on spontaneous shedding of sheep red blood cell binding receptors of T lymphocytes in vitro.

Nekam K, Varro R, Torok K, Lang I, Kalmar L, Gergely P, Petranyi G.

Many effects of transfer factor can be used for testing of its activity in vitro. Its effect on rosette formation has been utilized in two methods: the enhancement of rosetting of trypsin-treated T lymphocytes and the increase of 'active' rosettes depressed under some immunopathological conditions. 'Active' rosetting lymphocytes of healthy blood donors if kept at 37 degrees C for 4 hr shed partly their sheep red blood cell-binding receptors into the culture medium supplemented with 25% fetal calf serum. The adding of the negative skin test-converting fraction of dialysable leucocyte extracts inhibits the decrease of the number of rosettes. Possible explanations for the observed phenomenon are: transfer factor increases the rate of receptor synthesis, it causes uncovering or redistribution of the receptors, or it stabilizes otherwise shed membrane structures.

PMID: 6969967 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1977 Aug;29(2):261-5. Related Articles, Links

Crude transfer-factor preparations stimulate trypsinized human lymphocytes to form rosettes with sheep red cells.

Valdimarsson H, McGuire RL.

The binding sites for sheep red cells (E) on human lymphocytes are trypsin-sensitive but regenerate in vitro on incubation at 37 degrees C. The rate of this regeneration was increased in the presence of dialysates of human leucocyte extracts (DLE). Thus incubation of trypsinized lymphocytes for 3 hr in appropriate dilutions of DLE resulted in a 2- to 6-fold increase of E-binding activity above that observed in medium-incubated control lymphocytes. Dialysates prepared from human thymus and brain similarly accelerated recovery of E-binding activity whilst dialysates of human fibroblasts and liver cells were inactive. The regeneration of trypsinized membrane immunoglobulin was slightly delayed in the presence of DLE. These findings indicate that leucocyte dialysates contain an activity which preferentially stimulates the regeneration of a T-lymphocyte membrane component. It is suggested that this activity may account for the immunological restoration observed in some patients with T-lymphocyte deficiency after injection of leucocyte dialysates.

PMID: 302769 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1982 Jan;47(1):183-90. Related Articles, Links

Dual action of leucocyte dialysates and of thymosin on the recovery of sheep-cell-rosetting capacity in trypsinized human lymphocytes.

Sargent IL, Salaman MR, Valdimarsson H.

Trypsinization of human blood lymphocytes abolishes their capacity to form rosettes with sheep erythrocytes (E-rosettes) and this is regained in part on incubation of the cells at 37 degrees C for 3 hr. The recovery of rosetting capacity was found to be accelerated in the presence of dialysable extracts of human leucocytes (DLE) or bovine thymosin fraction 5 (THFV). For both DLE and THFV two types of effect were demonstrated. At lower concentrations the stimulation of recovery was dependent on the presence of the agent during incubation and it presumably comes about through an effect on the metabolic process required for regeneration of the E-receptors. At higher concentrations another mechanism is apparent since the agents were now effective when added after incubation. This last phenomenon is wholly dependent on prior incubation of the trypsinized lymphocytes in medium alone and it probably involves attachment of components of DLE and THFV to incompletely recovered cells, thereby providing a more favourable charge environment for E-rosette formation. A similar process of adhesion-promotion may be occurring in certain in-vitro tests with THFV which are carried out on lymphocytes from immunodeficient patients. On the other hand, it is the other mechanism, that of metabolic action, which is likely to be the predominant consideration in relation to treatment of such patients with DLE or THFV.

PMID: 7094423 [PubMed - indexed for MEDLINE]
Thymus. 1984;6(3):167-80. Related Articles, Links

Dialyzable leukocyte extracts contain thymosin.

Wilson GB, Paddock GV, Floyd E, Newell RT, Dopson MH.

Trypsinization of human T-lymphocytes removes surface receptors which bind to sheep erythrocytes (E). Human dialyzable leukocytes extracts (DLE) and thymosin (Fraction V) have been shown to significantly increase the rate of regeneration of T-lymphocyte E-receptors. Both physical-chemical and immunochemical results reported herein indicate that the enhancing effect of human DLE preparations on the rate of regeneration of T-lymphocyte E-receptors is due at least in part to the presence of thymosin alpha 1-peptide in these preparations. Thymosin alpha 1-peptide purified from thymosin Fraction V and putative thymosin alpha 1 preparations purified from human DLEs were each active not only in increasing the rate of regeneration of T-lymphocyte E-receptors removed by trypsinization but also were active in vitro in markedly increasing the number of E-rosetting cells in two patients with immunodeficiency disease manifested in part as a reduction in the normal percentage of mature T-lymphocytes capable of forming E-rosettes.

PMID: 6464097 [PubMed - indexed for MEDLINE]
Cell Immunol. 1979 Sep 15;47(1):1-18. Related Articles, Links

Bovine dialyzable lymph node extracts have antigen-dependent and antigen-independent effects on human cell-mediated immunity in vitro.

Wilson GB, Newell RT, Burdash NM.

PMID: 315822 [PubMed - indexed for MEDLINE]
Am J Vet Res. 1992 Jul;53(7):1225-30. Related Articles, Links

Effects of dialyzable lymph node extracts on lymphoblast proliferative capacity of blood mononuclear cells in cattle with chronic paratuberculosis.

Kreeger JM, Snider TG 3rd, Olcott BM.

Veterinary Medical Diagnostic Laboratory, College of Veterinary Medicine, University of Missouri, Columbia 65211.

Dialyzable lymph node extracts (DLE) containing transfer factor prepared from calves sensitized to Mycobacterium paratuberculosis and keyhole-limpet hemocyanin (KLH) were administered to 4 adult cows with chronic paratuberculosis. Cutaneous delayed hypersensitivity, lymphocyte blastogenesis, monocyte migration-inhibition, and lymphoblast proliferative capacity as a reflection of interleukin-2 (IL-2) activity were measured in response to M bovis purified protein derivative, johnin, and KLH before and after treatment with DLE. Change in cutaneous delayed hypersensitivity was not evident after DLE treatment. Alterations in histologic features of pre- and posttreatment sections of ileum and mesenteric lymph nodes were not detected. Lymph node extract treatment significantly (P less than 0.05) increased IL-2 activity and migration-inhibition in response to johnin and KLH in vitro. Treatment had no effect on lymphocyte blastogenesis. The data indicate that cattle with chronic paratuberculosis may benefit from DLE treatment, by virtue of increased IL-2 activity, and that effects of DLE are at least partially mediated by an increase in IL-2 activity.

PMID: 1497195 [PubMed - indexed for MEDLINE]
1: Clin Immunol Immunopathol. 1977 Sep;8(2):238-46. Related Articles, Links

Bovine transfer factor: in vivo transfer of cell-mediated immunity to cattle with alcohol precipitates.

Klesius PH, Fudenberg HH.

PMID: 902438 [PubMed - indexed for MEDLINE]
Infect Immun. 1982 Apr;36(1):271-6. Related Articles, Links

Transfer of Salmonella resistance and delayed hypersensitivity with murine-derived transfer factor.

Smith RA, Esa A, Stiff M.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&a...

Protective host immunity and delayed hypersensitivity were transferred to nonimmune ICR and C3H/HeJ mice with transfer factor prepared from the splenic lymphocytes of ICR Swiss mice immune to Salmonella typhimurium. Only mice

injected with the "immune" dialysate exhibited significant footpad swelling (P less than 0.01) to a spent medium antigen of S. typhimurium, but not Listeria monocytogenes. Host survival to a lethal Salmonella challenge infection was seen only in transfer factor-injected mice. Also, these challenged animals had fewer numbers of bacteria present in their spleens (P less than 0.01) than did challenged mice previously injected with either control dialysates or commercial endotoxin. Neither the Salmonella antigens nor endotoxin present in the sterile transfer factor preparation was responsible for the transfer of host protection and delayed hypersensitivity, since none of the control dialysates resulted in any positive responses when injected into either the ICR Swiss or endotoxin-resistant C3H/HeJ mice.

PMID: 7042572 [PubMed - indexed for MEDLINE]
Cell Immunol. 1986 Jul;100(2):555-62. Related Articles, Links

Specific transfer factor protects mice against lethal challenge with herpes simplex virus.

Viza D, Vich JM, Phillips J, Rosenfeld F, Davies DA.

Bovine transfer factor (TFd) specific to herpes simplex virus (HSV)1 or to HSV2 was prepared by immunizing calves with the corresponding virus. The TFd preparations were then injected into Swiss mice in an attempt to protect them against a subsequent lethal challenge with HSV1 or HSV2 virus. It was thus shown that injection of anti-HSV TFd protects the mice against the corresponding HSV virus, whereas the injection of a nonspecific TFd (anti-CMV) fails to protect against a challenge with HSV1. Furthermore, a dose-response effect was observed, since potent TFd preparations were ineffective when they were used at one-fifth of the original concentration. It seems, therefore, that animal models may be used to assay the potency of TFd preparations specific for herpes viruses.

PMID: 3019568 [PubMed - indexed for MEDLINE]
Acta Virol. 1992 May;36(3):239-44. Related Articles, Links

Chemical characterization of the purified component of specific transfer factor in the leukocyte dialysates from HSV-1 immunized goats.

Qi HY, Wan ZF, Su CZ.

Department of Biochemistry, Fourth Military Medical University, Xian, Shaan Xi, P.R. China.

The chemical characterization of the purified component responsible for HSV-1 specific transfer factor activity (PTFC) by high resolution analytical methods was performed. PTFC had a molecular weight of 6,000 dalton by the size-exclusion HPLC analysis; it showed a marked UV-absorbance spot at 254 nm and a fluorescent spot at 366 nm on the thin-layer plate by thin-layer chromatography which spots coincided at the same place of the plate. The amino acid composition and sequencing analyses showed that PTFC consisted of at least twelve different amino acids, but the amino acid sequence could not be determined. The combined results indicate that PTFC is a compound with a molecular weight of 6,000 dalton, composed of peptide and nucleotide-like material. The peptide is rich in aspartic acid and its N-terminal end may be blocked.

PMID: 1360751 [PubMed - indexed for MEDLINE]
J Allergy Clin Immunol. 1976 Jul;58(1 PT. 2):190-7. Related Articles, Links

Transfer factor: hypoxanthine is a major component of a fraction with in vivo activity.

Tomar RH, Knight R, Stern M.

Transfer factor was prepared from the leukocyte lysates of four donors with known skin test reactivity. After ultrafiltration and double-gel filtration on polyacrylamide gels, fraction IV of the preparation was found to have biologic activity. This fraction contained one major and occasionally one minor ultraviolet-absorbing and zero to one ninhydrin-detectable spots on thin-layer chromatography. The major ultraviolet spot was identified as hypoxanthine. Hypoxanthine was demonstrated to be responsible for the high 260 nm/280 nm ratio of preparations with biologic activity in vivo. It was not determined if hypoxanthine is required for transfer factor activity. In addition, an orcinol-negative preparation also had biologic activity.

PMID: 956555 [PubMed - indexed for MEDLINE]
Proc Natl Acad Sci U S A. 1974 February; 71(2): 498–502.

Chemotactic Activity in Dialyzable Transfer Factor
John I. Gallin and Charles H. Kirkpatrick

Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20014

Abstract

Dialyzable transfer factor from human leukocytes was found to be strongly chemotactic for granulocytes and weakly chemotactic for monocytes in vitro. Chemotactic properties were also demonstrated in vivo in rhesus monkey skin. Initial purification of the dialyzable transfer factor by Sephadex G-25 chromatography revealed multiple fractions containing material with 255-nm absorbance. The fractions containing chemotactic activity were also capable of transferring delayed hypersensitivity to rhesus monkeys. This chemotactic material has an apparent molecular weight of 5000 daltons or less and was not inactivated by goat antibody to components C3 or C5 of human complement; chemotactic activity was lost after storage for two weeks at 4° and the activity of two of three preparations was decreased by heating for 30 min at 56°. This previously undescribed chemotactic activity of dialyzable transfer factor may have significance in relation to cell-mediated immune responses.
granulocytes | monocytes | immune response | lymphokines | primate | delayed hypersensitivity

Lancet. 1973 Oct 13;2(7833):822-3. Related Articles, Links

What is transfer factor?

Gottlieb AA, Foster LG, Waldman SR, Lopez M.

PMID: 4126619 [PubMed - indexed for MEDLINE]
J Reticuloendothel Soc. 1977 Jun;21(6):403-16. Related Articles, Links

Biochemical analysis of dialyzable leukocyte extracts.

Gottlieb AA, Saito K, Sutcliffe S, Foster LA, Tamaki N, Maziarz G, Sutherland C, Brennessel B.

PMID: 886545 [PubMed - indexed for MEDLINE]

The effects of dialyzable products from human leukocyte extracts on cutaneous delayed-hypersensitivity response.

Gottlieb AA, Maziarz GA, Tamaki N, Sutcliffe SB.

Fractions from human whole leukocyte lysates were prepared by sequential double dialysis against membranes with cut-offs of m.w. 12,000 and 3500, and by elution chromatography on Sephadex G-10. The effect of localized intracutaneous implantation of fractions with m.w. less than 3500 was studied. Two types of response were obtained: 1) the amplification of response to antigen to which the donor had preexisting immunity, and 2) the induction of inflammatory response histologically resembling delayed hypersensitivity in the absence of added antigen. The substances mediating these responses could be separated into unique components by use of a long (1 x 150 cm) G-10 column, or by hydroxylapatite chromatography. The active principles were derived from leukocyte extracts (as demonstrated by their absence from autologous RBC extracts prepared by identical methodology), and the histopathologic appearances after intracutaneous implantation were compatible with those of a delayed-hypersensitivity response. No evidence of transfer of antigen-specific information from a sensitive donor to a nonsensitive recipient was obtained under the conditions of study.

PMID: 7356716 [PubMed - indexed for MEDLINE]
Acta Virol. 1985 Jan;29(1):25-34. Related Articles, Links

Antigen-specific transfer factor from mice immunized with an attenuated flavivirus: augmentation of inducing activity in semipurified splenocytic dialyzates.

Mayer V, Gajdosova E, Valaskova M, Oravec C.

Three large batches were prepared of lyzed splenocytic leukocyte dialyzate from SPF outbred mice, immunized with a live attenuated virus from the tick-borne encephalitis (TBE) complex. Total mass of freeze-dried dialyzates was 1.73 g. One mg of respective batches contained 2 X 10(5), 2 X 10(4) and 2 X 10(3) units of the transfer factor, specific for the flavivirus group-antigen, as estimated according to the capacity to induce specifically cytotoxic T-cells in the recipient C3H mice.

The amount of protein and orcinol-reactive material (purine-bound ribose), the presumed components of the inducer's substrate, ranged in individual dialyzates from 9.9-12.4 and 0.72-0.80% of their dry mass. Materials from each batch obtained after double precipitation by ethanol were subjected to permeation chromatography on Sephadex G-25 columns and subsequent lyophilization of the peak with specific inducing activity. The final product represented on average 3.7 per cent of dry mass of the starting material. In comparison to the crude material, in one mg of the final product the protein and the orcinol-reactive material were reduced by 80 and 37 per cent, respectively, but an increment in the antigen-specific inducing capacity comprising 2-3 log10 units was observed. These findings add to the concept that a) macromolecules carrying the inducing activity can be separated from other constituents of the crude dialyzate and b) an increase in antigen-specific inducing activity titre was, besides partial concentration, mainly due to removal of suppressor or inhibitory factor(s) present in the crude dialysates and probably acting in vivo.

PMID: 2859759 [PubMed - indexed for MEDLINE]
Acta Virol. 1982 Dec;26(6):453-65. Related Articles, Links

Dialysable specific transfer factor in mice immunized with attenuated Langat virus from the tick-borne encephalitis complex: generation, action and quantitative assay.

Mayer V, Gajdosova E, Valaskova M, Gombosova A, Oravec C.

Cytolytic T lymphocyte assay was developed in order to measure the response of inbred C3H mice to dialysable specific transfer factor (STF), induced in subadult outbred mice by one shot immunization with the attenuated Langat virus. The first STF activity in mice splenic leukocytes was detected between 48-72 hr after virus administration. The conversion of splenic T-cell cytotoxic response in C3H mice in vivo occurred between 15-21 hr after STF administration. The killing activity of T-cells, induced by STF, showed cross-reactive traits within the genus Flavivirus. STF, given prior to the live virus, augmented the specific cytolytic T-cell response. In the live virus-primed mice the booster effect was markedly enhanced when administration of STF preceded the second immunization dose. In the serum of STF recipients, interferon was irregularly detected attaining low levels for short time periods. Temperature of 56 degrees C for 60 min abolished the activity of least 10(4) murine STF units, temperature of 37 degrees C lowered after 24 hr this activity by 3 log10units. Chromatography of the dialyzed leukocyte lysate on Sephadex G-25 column yielded usually five peaks. The second peak showed an increased content of ribose-bound and protein materials and, as a rule, a relatively concentrated STF activity.

PMID: 6188353 [PubMed - indexed for MEDLINE]
Acta Virol. 1980 Dec;24(6):459-63. Related Articles, Links

Transfer with dialysable transfer factor of T-lymphocyte cytolytic response to tick-bone encephalitis virus antigen in naive mice.

Mayer V, Gajdosova E, Oravec C.

Transfer factor activity was demonstrated in the dialysable extract from lymphocytes from outbred donor mice, in which immunization with live attenuated Langat (E5 "14") virus induced a stage of high resistance against challenge with virulent tick-borne encephalitis virus. Administered to naive inbred recipient mice, the extract conveyed in them specific cytolytic activity, exerted by their T lymphocytes, as demonstrated by the 51Cr release assay on tick-borne encephalitis virus-infected syngeneic L-929 cells.

PMID: 6111208 [PubMed - indexed for MEDLINE]
Zh Mikrobiol Epidemiol Immunobiol. 1998 Mar-Apr(2):83-5. Related Articles, Links

[The immunomodulating activity of a transfer-factor preparation transflavin, specific to tick-borne encephalitis virus]

[Article in Russian]

Iushkova TA, Iushkov VV.

Transflavin, a transfer-factor preparation specific to tick-borne encephalitis virus, was experimentally shown to possess immunomodulating action. The immunomodulating action of this preparation could be observed in a dose of 1 D (1 D being equivalent to 5 x 10(8) lymphocytes), which was manifested by an increase in the phagocytic activity of neutrophils and macrophages, a rise in the amount of T-lymphocytes, an increase in rosette formation, the number of antibody-forming cells, increased proliferation on T- and, to a lesser extent, B-cell mitogens, the restoration of the T-dependent expression of lymphocyte receptors, inhibited by trypsin. Transflavin in doses of 0, 1 and 10 D suppressed primary immune response. The probable mechanisms of the immunomodulating action of the Transflavin under study is discussed.

PMID: 9662809 [PubMed - indexed for MEDLINE]
Acta Virol. 1993 Feb;37(1):109. Related Articles, Links

Specific inducer factor purified from splenocytic dialyzates of goat immunized with Japanese encephalitis virus.

Song C, Li B, Wu W.

Publication Types:
• Letter

PMID: 8105646 [PubMed - indexed for MEDLINE]
Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 1983 Feb;5(1):47-50. Related Articles, Links

[Effect of Japanese encephalitis virus-specific transfer factor on adherent inhibitory activity of peritoneal exudate cells]

[Article in Chinese]

Wang FZ, Huang ZX.

PMID: 6226386 [PubMed - indexed for MEDLINE]
Ann Intern Med. 1976 Jun;84(6):708-9. Related Articles, Links

Chronic pulmonary histoplasmosis: improved lymphocyte response with transfer factor.

Smith CR, Griffin DE, Graybill JR.

Publication Types:
• Case Reports

PMID: 937885 [PubMed - indexed for MEDLINE]
Kansenshogaku Zasshi. 1989 Dec;63(12):1329-32. Related Articles, Links

[Effects of transfer factor on chronic hepatitis B in childhood]

[Article in Japanese]

Iseki M, Aoyama T, Koizumi Y, Ojima T, Murase Y, Osano M.

Nine children, 1 to 13 years of age, with HBeAg positive chronic hepatitis B received transfer factor (T.F.) monotherapy for 3 to 17 months, and were monitored by check-ups every six months from serum HBeAg, anti-HBe and GPT. In 12 months, 4 subjects became HBeAg negative and had normal serum GPT. In 22 to 48 months, 6 of the nine subjects had negative HBeAg and normal GPT, 2 had positive HBeAg and high GPT values. The remaining 1 subject who was observed for six months after T.F. therapy remained HBeAg positive with a high GPT values. No side effects were observed. These preliminary observations may indicate beneficial effects of T.F. on the natural course of chronic hepatitis B in childhood, though the ultimate effects awaits longer and well controlled clinical trials.

PMID: 2621386 [PubMed - indexed for MEDLINE]
Acta Paediatr Jpn. 1991 Jun;33(3):327-34. Related Articles, Links

Combination therapy with transfer factor and high dose stronger neo-minophagen C in chronic hepatitis B in children (HBe Ag positive).

Sumiyama K, Kobayashi M, Miyashiro E, Koike M.

Department of Pediatrics, Wakayama Medical College, Japan.

This study mainly describes the efficacy of the combination therapy with Transfer Factor (TF) and high dose Stronger Neo-Minophagen C (SNMC) for HBV carrier children with HBe Ag positive chronic hepatitis. There were 12 patients, 10 males and 2 females aged from 7 months to 14 years 8 months. Liver biopsy was done in 11 patients, and the

histopathological findings of the liver were chronic active hepatitis (8 cases) and chronic inactive hepatitis (3 cases). In 6 of 8 patients, HBe-Ag became negative (75%) within 18 weeks (mean 8 weeks) after the initiation of the combination therapy with TF and SNMC (HBe-seronegative), and 4 of these 8 patients (50%) became anti-HBe positive within 29 weeks (mean 15 weeks) (HBe-seroconversion). These results suggest that combination therapy with TF and high dose SNMC may be beneficial in the treatment of chronic hepatitis B in children.

PMID: 1785328 [PubMed - indexed for MEDLINE]
Cancer. 1997 Apr 15;79(8):1494-500. Related Articles, Links

The long term efficacy of glycyrrhizin in chronic hepatitis C patients.

Arase Y, Ikeda K, Murashima N, Chayama K, Tsubota A, Koida I, Suzuki Y, Saitoh S, Kobayashi M, Kumada H.

Department of Gastroenterology, Tonanomon Hospital, Minato-ku, Tokyo, Japan.

BACKGROUND: Hepatocellular carcinoma (HCC) occurs in patients with hepatitis C virus-RNA positive chronic liver disease. It is important to prevent HCC with drug administration. METHODS: A retrospective study was undertaken to evaluate the long term preventive effect of Stronger Neo-Minophagen C (SNMC) on HCC development. SNMC is a Japanese medicine that is commonly administered to patients with chronic hepatitis C to improve the serum alanine aminotransferase (ALT) level. Of 453 patients diagnosed with chronic hepatitis C retrospectively in the study hospital between January 1979 and April 1984, 84 patients (Group A) had been treated with SNMC; SNMC was given at a dose of 100 mL daily for 8 weeks, then 2-7 times a week for 2-16 years (median, 10.1 years). Another group of 109 patients (Group B) could not be treated with SNMC or interferon for a long period of time (median, 9.2 years) and were given other herbal medicine (such as vitamin K). The patients were retrospectively monitored, and the cumulative incidence of HCC and risk factors for HCC were examined. RESULTS: The 10th-year rates of cumulative HCC incidence for Groups A and B were 7% and 12%, respectively, and the 15th-year rates were 12% and 25%. By Cox regression analysis, the relative risk of HCC incidence in patients not treated with SNMC (Group B) was 2.49 compared with that of patients treated with SNMC (Group A). CONCLUSIONS: In this study, long term administration of SNMC in the treatment of chronic hepatitis C was effective in preventing liver carcinogenesis.

PMID: 9118029 [PubMed - indexed for MEDLINE]
: Nippon Rinsho. 1994 Jul;52(7):1823-7. Related Articles, Links

[Efficacy of interferon combined glycyrrhizin therapy in patients with chronic hepatitis C resistant to interferon therapy]

[Article in Japanese]

Okuno T, Arai K, Shindo M.

Department of Internal Medicine, Akashi Municipal Hospital.

To assess the efficacy of interferon (IFN) combined with a large dose of glycyrrhizin (SNMC) therapy in patients with chronic hepatitis C who were resistant to interferon therapy alone, we studied 8 patients with chronic hepatitis C who did not respond to the initial interferon therapy. Initially all of 8 patients received 6 million units of alpha-IFN intramuscularly, three times a week, for 3 months and their serum alanine transaminase (ALT) did not decrease more than 50% at the end of therapy and returned to pretreatment levels after therapy. Six months later, all of these patients received alpha-IFN (6 MU) combined with 80 ml of SNMC intravenously, three times a week for 6 months. Prior to the initial IFN therapy alone, all of the patients were positive for anti-HCV and HCV RNA in the serum. With IFN therapy, serum HCV RNA became negative in 4 of 8 patients and HAI score decreased significantly although their ALT levels did not decrease more than 50%, while with IFN combined with SNMC therapy, ALT levels decreased approximately 70% in all patients (one became normal), serum HCV RNA became negative in 2 and HAI scores did not change significantly. There was no significant differences in decrease of HCV RNA titers and HAI scores between two therapy except the ALT levels. These findings suggest that IFN combined SNMC therapy does not appear to be more beneficial than IFN therapy alone.

Publication Types:
• Review
• Review, Tutorial

PMID: 8078202 [PubMed - indexed for MEDLINE]
N Engl J Med. 1979 Jun 7;300(23):1332. Related Articles, Links

Transfer factor for the treatment of chronic acute hepatitis.

Pizza G, Viza D, Roda A, Aldini R, Roda E, Barbara L.

Publication Types:
• Letter

PMID: 440338 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1979 May;36(2):221-6. Related Articles, Links

Transfer factor and hepatitis B: a double blind study.

Ellis-Pegler R, Sutherland DC, Douglas R, Woodfield DG, Wilson JD.

A prospective, double blind placebo-controlled trial was carried out on twenty-nine patients with hepatitis B. Thirteen received transfer factor and sixteen placebo. There were no significant differences between the two groups in any clinical or laboratory measurements made, although a rapid early reduction of serum aspartate transaminase levels by transfer factor is possible. Similarly, no significant changes were delineated by the in vitro measurements of lymphocyte function. Transfer factor did not alter the natural course of hepatitis B.

Publication Types:
• Clinical Trial
• Controlled Clinical Trial

PMID: 477025 [PubMed - indexed for MEDLINE]
Proc Soc Exp Biol Med. 1985 Mar;178(3):468-75. Related Articles, Links

Transfer factor for the treatment of HBsAg-positive chronic active hepatitis.

Roda E, Viza D, Pizza G, Mastroroberto L, Phillips J, De Vinci C, Barbara L.

Transfer factor was obtained from four patients having recovered from acute type-B viral hepatitis. It was replicated in vitro using the LDV/7 lymphoblastoid cell line. This in vitro-produced transfer factor specific for hepatitis B (TFdL-H) was administered to 10 randomly selected patients with biochemically and histologically proven HBsAg-positive chronic active hepatitis (CAH) at 15-day intervals over a 6-month period. In three out of four initially HBeAg-positive patients, anti-HBe antibodies appeared when the HBeAg disappeared. In one of these patients and in two other HBsAg-positive patients, the appearance of anti-HBs antibodies was noted. The improvement in several biochemical parameters of the TFdL-H patients was statistically significant when compared with those of another group of 10 randomly selected untreated CAH patients. Liver biopsies in six out of eight treated patients showed a histological improvement at the end of the treatment. These results suggest that TFdL-H may be used with beneficial effect for the treatment of HBsAg-positive CAH.

Publication Types:
• Clinical Trial

PMID: 3883364 [PubMed - indexed for MEDLINE]
Clin Exp Immunol. 1977 Oct;30(1):10-5. Related Articles, Links

Transfer factor in the attempted treatment of patients with HBsAg-positive chronic liver disease.

Jain S, Thomas HC, Sherlock S.

Six patients with hepatitis B surface antigen-positive (HBsAg-pos) chronic liver disease have been treated with transfer factor (TF) prepared from leucocytes of normal blood donors with no history of hepatitis, and with TF from subjects recently recovered from type B hepatitis. In three patients there were transient elevations of aspartate transaminase (AsT) after 'specific' TF, representing damage or destruction of hepatocytes, and in two of these patients there was coincidental complement consumption, suggesting that TF had stimulated production of antibody. In one other patient there was an increase in E-rosetting lymphocyte (ERL) concentration representing a change in T-lymphocyte reactivity. One of the two patients who had no measured response to TF had a primary liver cell carcinoma and was receiving prednisolone therapy. TF prepared from subjects who have recently recovered from type B hepatitis may have temporarily altered the immunological status of patients with HBsAg-pos chronic liver disease, but it did not have a beneficial therapeutic effect.

PMID: 606432 [PubMed - indexed for MEDLINE]