# Abstracts on studies conducted with Transfer factors from bovine colostrum

บทคัดย่อการศึกษาTransfer Factor บางส่วน จากน้ำนมเหลืองของวัว


## Transfer factor helps the body recognize antigens.
## (Transfer Factor ช่วยให้ร่างกายรับรู้สิ่งแปลกปลอมอย่างมากมาย)

**Feb 1, 2003**
By: Kenneth Marcella, DVM
DVM Newsmagazine

Dr. M. Metz, a veterinarian consulting for 4LifeResearch, the company which has the patent for extracting transfer factor from colostrum, **points out that 200 mg (one capsule) of transfer factor has the potential for recognizing at least 100,000 pathogens.** Metz adds that not only can transfer factor be specific for an individual antigen that a lymphocyte is exposed to, but **"transfer factor can also stimulate a multivalent response." In this type of response, transfer factor activates lymphocytes to several strains of an organism.**
"This is the really exciting part of transfer factor from a practicing veterinary standpoint," says Metz.
4LifeResearch has found that by exposing cattle to various bacteria and viruses they can produce transfer factor that will stimulate immunity to other related strains of bacteria and viruses that are much more pathogenic to other species.
**"The other really exciting aspect of transfer factor," says Metz, "is the time sequence."**
**Most types of delayed hypersensitivity immunity, such as that seen with vaccine use, take 10 to 14 days to develop. Transfer factor, according to Metz, activates that same immunity in 24 hours!**

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## TRANSFER FACTOR IN TREATMENT OF MULTIPLE SCLEROSIS
## (ระบบส่วนกลางเสื่อม)


- A. Basten, J.D. Pollard, G.J. Stewar, J.A. Frith, J.G. Mcleod, J.C. Walsh, R. Garrick, C.M. Van Der Brink
- Department of Medicine, University of Sydney,, United Kingdom and Departments of Clinical Immunology and Neurology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia


- Available online 26 September 2003.


# Abstract


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 until 18 months after the start of the trial; and (3) treatment was effective only in those patients with mild to moderate disease activity.


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Mol Med **2000** Apr;6(4):332-41

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

## (ศึกษาโมเลกุลของ ทรานสเฟอร์ แฟกเตอร์)

**Kirkpatrick CH.**
Department of Medicine, University of Colorado Health Sciences Center, Denver, USA.

BACKGROUND: Transfer factors are small proteins that "transfer" the ability to express cell-mediated immunity from immune donors to non-immune recipients. We developed a process for purifying specific transfer factors to apparent homogeneity. This allowed us to separate individual transfer factors from mixtures containing several transfer factors and to demonstrate the antigen-specificity of transfer factors.

Transfer factors have been shown to be an effective means for correction of deficient cellular immunity in patients with opportunistic infections, such as candidiasis or recurrent Herpes simplex and to provide prophylactic immunity against varicella-zoster in patients with acute leukemia.

MATERIALS AND METHODS: Transfer factors of bovine and murine origin were purified by affinity chromatography and high performance liquid chromatography. Cyanogen bromide digests were sequenced. The properties of an apparently conserved sequence on expression of delayed-type hypersensitivity by transfer factor recipients were assessed.

RESULTS: A novel amino acid sequence, LLYAQDL/VEDN, was identified in each of seven transfer factor preparations. These peptides would not transfer expression of delayed-type hypersensitivity to recipients, which indicates that they are not sufficient for expression of the specificity or immunological properties of native transfer factors. However, administration of the peptides to recipients of native transfer factors blocked expression of delayed-type hypersensitivity by the recipients. The peptides were not immunosuppressive.

CONCLUSIONS: These findings suggest that the peptides may represent the portion of transfer factors that binds to the "target cells" for transfer factors. Identification of these cells will be helpful in defining the mechanisms of action of transfer factors.

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# Environmental processes affecting plant root uptake of radioactive trace elements and variability of transfer factor data: a review

## (การดูดซึม)

- Sabine Ehlken[1], Gerald Kirchner Department of Physics/FB 1, University of Bremen, Postfach 330440, D-28334 Bremen, Germany.
- Received 3 July 2000. Revised 22 September 2000. Accepted 22 September **2000**.
- Available online 5 November 2001.

## Abstract

Soil-to-plant transfer factors are commonly used to estimate the food chain transfer of radionuclides. Their definition assumes that the concentration of a radionuclide in a plant relates linearly solely to its average concentration in the rooting zone of the soil. However, the large range of transfer factors reported in the literature shows that the concentration of a radionuclide in a soil is not the only factor influencing its uptake by a plant. With emphasis on radiocesium and -strontium, this paper reviews the effects of competition with major ions present in the soil-plant system, the effects of rhizosphere processes and soil micro-organisms on bioavailability, the factors influencing transport to and uptake by roots and the processes affecting long-term uptake rates. Attention is given to summarizing the results of recent novel electrophysiological and genetic techniques which provide a physiologically based understanding of the processes involved in the uptake and translocation of radiocesium and -strontium by plants.

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Biotherapy **1996**;9(1-3):133-8

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

**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

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Biotherapy **1996**;9(1-3):61-6

## Efficacy of transfer factor in treating patients with recurrent ocular herpes infections.
## (ผู้ป่วยติดเชื้อซ้ำ)

**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

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Biotherapy **1996**;9(1-3):87-90

## Lessons from a pilot study of transfer factor in chronic fatigue syndrome.
## (อ่อนเพลียเรื้อรัง)

**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 placebocontrolled 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

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Biotherapy **1996**;9(1-3):81-6

## Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome
## (อ่อนเพลียเรื้อรัง)
### (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 onepatient 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.

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Biotherapy **1996**;9(1-3):41-7

## Preliminary observations using HIV-specific transfer factor in AIDS.
## (ผู้ป่วย HIV)

**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

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## *Abstract*: 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.
## (อักเสบเรื้อรัง, อ่อนเพลียเรื้อรัง)

**Biotherapy 1996; 9(1-3): 91-5**

Abstract
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.
Source: www.ahmf.org

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## *Abstract*: The use of *transfer factor*s in chronic fatigue syndrome: prospects & problems Levine PH.
## (อ่อนเพลียเรื้อรัง)

**Biotherapy 1996; 9(1-3): 77-79**

Abstract
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.
Source: www.ahmf.org

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## *Abstract*: Activities and Characteristics of *transfer factors* (การทำงานของ ทรานสดฟอร์ แฟกเตอร์)

ImmuneSupport.com 12-12-2000

**Biotherapy 1996;9(1-3):13-6**

Kirkpatrick, C.H.

This report summarizes three components of our transfer factor research program. Several clinical studies have used oral administration of transfer factor containing materials. Sceptics have rejected these findings by assuming that the acidic and enzymatic environment of the gastrointestinal tract would destroy the factors.

To further examine this issue, we have conducted dose-response studies of the delayed-type hypersensitivity reaction in mice that were given transfer factor either by gavage or subcutaneously. There were no differences in the responses that were related to the route of administration. We conclude that oral route of administration is efficacious and should be used when possible. We have also studied the effects of transfer factors on immune responses by recipients.

The details of this research are presented in the paper by Dr. Alvarez-Thull. Briefly, the study showed that recipients of a specific transfer factor responded to the antigen for which the factor was specific by secreting gamma-IFN, but no other cytokines. The structures of transfer factor molecules are unknown. We have developed a process for isolating transfer factors in pure form and we have obtained preliminary data concerning amino acid sequences. Our goal is to obtain the complete primary structure of several transfer factor molecules.

PMID: 8993752, UI: 97146896

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## Transfer factor (diffusing capacity) standardized for alveolar volume: validation, reference values and applications of a new linear model to replace KCO (TL/VA)

Eur Respir J. **1996** Jun;9(6):1269-77. http://www.ncbi.nlm.nih.gov/pubmed/8804948

**DJ Chinn, JE Cotes, R Flowers, AM Marks and JW Reed**

### Abstract

Transfer factor (TL) varies with alveolar volume (VA), but not in the manner implied by the carbon monoxide transfer coefficient (KCO (TL/VA)). This paper considers two other simple models (one linear and one exponential) which might standardize TL for VA, and asks the questions: 1) Is either model valid? 2) What are appropriate reference values? and 3) Will the model be useful? The relationship of TL to VA within subjects at different depths of inspiration, and between subjects having lungs of different sizes, were measured and compared. The subjects were asymptomatic, nonsmoking, Caucasian adults, including 31 males assessed in the laboratory and 503 male and female participants in population studies. The linear partial regression coefficients of TL on VA (L corrected for body temperature, atmospheric pressure and water saturation (BTPS)) standardized for height (H) in metres, were similar within- and between-subjects; the coefficients applied over a wide range of values for VA. This was not the case for the exponential model. The resulting reference equations in SI units for males and females were: TL = 11.52 H + 2.72 VA.H-2 - 0.051 Age -12.35. RSD 1.17; and TL = 4.87 H + 2.29 VA.H-2 - 0.019 Age -3.03. RSD 0.92, respectively. The residual standard deviations (RSD) about the new relationships were less than in other series. The new linear model could account for much of the variation between different published reference values for TL; it could be useful clinically, in circumstances when VA deviates from the norm. The model does not explain differences in TL associated with gender. Inclusion of VA.H-2 as a covariate in the reference equation for transfer factor, in addition to age and height, improves the accuracy of prediction of normal transfer factor compared with current reference values; its use suggests that some of the differences between published values is due to the volume term. The equations can be used clinically, and eliminate the need for carbon monoxide transfer coefficient.

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## Structural nature and functions of transfer factors. (โครงสร้างและการทำงาน ของ Transfer Factor)

Ann N Y Acad Sci **1993** Jun 23;685:362-8

**Kirkpatrick CH.**

Conrad D. Stephenson Laboratory for Research in Immunology, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.

Transfer factors are molecules that "educate" recipients to express cell-mediated immunity. This effect is antigen-specific. The most consistent effects of transfer factors on the immune system are expression of delayed-type hypersensitivity and production of lymphokines such as macrophage migration inhibitory factor (MIF), which is probably identical to gamma-interferon in response to exposure to antigen. Transfer factors bind to antigens in an immunologically specific manner. This discovery has enabled us to isolate individual transfer factors from mixtures that contain several transfer factors. This reactivity probably explains the specificity of individual transfer factors, and it has provided a method for purification of individual transfer factors to apparent homogeneity. The purified materials are immunologically active and antigen-specific. They have molecular weights of approximately 5,000 Da and appear to be composed entirely of amino acids. Transfer factors appear to offer a novel means of molecular immunotherapy for certain patients with defective cell-mediated immunity.
Publication Types:

Review, tutorial

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## *Abstract*: Purification of transfer factors
### (การทำทรานสเฟอร์ แฟกเตอร์ ให้บริสุทธิ์)

Mol Immunol **1992** Feb;29(2):167-82 PMID: 1542296, UI: 92178226
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.

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Anticancer Res **1990** Sep-Oct;10(5A):1183-7

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

**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

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Ann Allergy **1989** Mar;62(3):170-6

## Biological response modifiers. Interferons, interleukins, and transfer factor.
### (การตอบสนองทางชีวภาพ)

**Kirkpatrick CH.**
Department of Medicine, National Jewish Center for Immunology and Respiratory Medicine, Denver,
Colorado.

Natural consequences of knowledge of the mechanisms that regulate immune responses are the attempts to modify the immune system in order to increase resistance to infectious diseases and to enhance activity against tumor cells. This review describes the roles of interferons and interleukins in
immune responses and reviews the experience with transfer factor in treatment of certain diseases.
Publication Types:

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Acta Virol **1988** Jan;32(1):6-18

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

**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.

## Treatment of cryptosporidiosis with oral bovine transfer factor
## (การถ่ายโอนในช่องปากวัว)


- E. Louie[a], W. Borkowsky[a], P.H. Klesius[*], T.B. Haynes[*], S. Gordon[a], S. Bonk[a], H.S. Lawrence[a]
- New York University Medical Center, New York, New York 10016, USA [b] USDA ARS Animal Parasite Research Laboratory, Auburn, Alabama 36830 USA. Received 20 January 1987.


- Accepted 15 April 1987.


# Abstract


Cryptosporidia are intestinal protozoans long known to cause diarrhea in humans, especially those with acquired immune deficiency syndrome (AIDS). When transfer factor prepared from calves which possessed delayed-type hypersensitivity to *Eimeria bovis* was given to nonimmune calves and mice it conferred protection against clinical infection (coccidiosis). Recent studies with oral bovine transfer factor have shown that it can confer cell-mediated immunity to humans. Based on these findings we decided to treat eight AIDS patients suffering from *Cryptosporidium*-associated diarrhea with transfer factor prepared from calves immune to *Cryptosporidium*- Prior to treatment with transfer factor, three patients had been treated with spiramycin, one patient with α-difluoromethylornithine (DFMO), and one patient with furazolidone for greater than 1 month without clinical or laboratory improvement. Following administration of transfer factor, five or eight patients exhibited a decrease in the number of bowel movements and the development of formed stools. *Cryptosporidium* was eradicated from the stools of four patients but two of these patients subsequently relapsed and one patient continued to have diarrhea despite the absence of *Cryptosporidium* in the stool. One patient has been free of diarrhea and *Cryptosporidium* for 2 years after discontinuation of transfer factor therapy.

Informed consent was obtained from the patients or their parents or guardians. Guidelines for human experimentation of the Institutional Review Board of NYU Medical Center were followed in conducting the clinical research.


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Am J Vet Res **1985** Apr;46(4):875-8


## Delayed-type hypersensitivity responses induced by bovine colostral components.
## (ภูมิแพ้แบบช้า)


**Radosevich JK, Scott GH, Olson GB.**



Transfer factor-type substances obtained from leukocytic cells and fluid portions of bovine colostrum caused effective passive transfer of delayed-type hypersensitivity responses across species barriers. Passive transfer of Brucella abortus sensitivity was obtained with equal regularity when usingcomponents derived from peripheral blood and colostrum of dams sensitized at 3 and 9 months of age. Colostral feedings to calves caused the passive transfer of delayed-type hypersensitivity as early as 2 days after parturition. The findings indicated that colostral components were important in the process ofcell-mediated immunity.


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Cell Immunol **1984** Nov;89(1):259-64


## Transfer factor and repeated otitis media.
## (หูชั้นกลางอับเสบซ้ำ)


**Kaminkova J, Lange CF.**



The effect of transfer factor (TF) was investigated in 12 children with repeated otitis media. These patients were immunologically compared to a control group of 23 age-matched healthy children. Levels of immunoglobulins, total and "active" T-cells, and phagocytic activity of granulocytes and monocytes were

evaluated in the 12 children prior to, during, and after TF therapy. Percentages of "active" T cells and absolute numbers of "active" T and total T cells, which were initially low in the patient group, increased significantly after TF therapy to statistically match those of the healthy control group.
The percentage of phagocytic monocytes in patients after therapy did not differ from healthy children; however, the percentage of phagocytic granulocytes remained depressed significantly. The levels of IgG, IgA, and IgM were unaffected by the therapy although the IgA and IgM were higher in the patient population throughout the study. After therapy, one-half of the patient population remained asymptomatic for a 1-year period and the others had markedly reduced attack rates.

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Thymus **1982**;4(6):335-50

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

### (การตอบสนองต่อเม็ดเลือดขาว)

**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 PPDspecific 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.

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## Deletion of antigen-specific activity from leukocyte dialysates containing transfer factor by antigen-coated polystyrene.

**J Immunol. 1981 Feb;126(2):486-9**
**W Borkowsky and H S Lawrence J Immunol 1981 126:486-9**

### Abstract

We have reported finding antigen-specific activity in human leukocyte dialysates (DLE) containing TF in the leukocyte migration inhibition (LMI) assay. To analyze this activity further, we have used polystyrene bound to antibody or to antigen as immunoadsorbent for DLE before pulsing nonimmune cells in the LMI assay. Candida-(CAN) immune or diphtheria toxoid-(TOX) immune DLE were depleted of all antigen-specific activity after absorption with specific antigen but not affected by absorption with specific antibody, respectively, and depletion of activity with antigen was abrogated by coating bound antigen with specific antibody before absorption of DLE. CAN-immune, TOX-immune DLE was selectively depleted for either CAN activity or TOX activity after absorption with CAN- or TOX-coated polystryrene, respectively, retaining its CAN-activity when absorbed with TOX and conversely retaining its TOX activity when absorbed with CAN; thus the antigen-specific activity binds to related but not unrelated antigen. The polystyrene-bound antigen-specific activity could be recovered by treatment with 8 M urea. We interpret these findings to suggest that such antigen-specific activity may be either a dialysable fragment of a T cell antigen receptor site, or a portion of the V-region, or a unique Ir gene product that assists in antigen presentation to other T cells.



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Lancet **1981** Jul 18;2(8238):122-4

# Treatment of childhood combined Epstein-Barr virus/cytomegalovirus infection with oral bovine transfer factor.

## (โรคในวัยเด็ก Epstein-Barr virus)

**Jones JF, Minnich LL, Jeter WS, Pritchett RF, Fulginiti VA, Wedgwood RJ.**

An illness lasting for two years, with recurrent fever, rash, abdominal pain, and arthralgia, developed in a four year old boy.
He was found to have a combined Epstein-Barr virus and cytomegalovirus (CMV) infection. His symptoms, CMV in his urine, and an absent in vitro lymphocyte response to CMV antigen persisted for two years. After treatment with orally administered bovine transfer factor clinical symptoms and viruria disappeared and specific immunity to CMV developed. Evaluation of this treatment in chronic virus infections is warranted.

# Transfer Factor for the Prevention of Varicella-Zoster Infection in Childhood Leukemia

## (โรคงูสวัด และมะเร็งในเม็ดเลือดขาว)

Russell W. Steele, M.D., Martin G. Myers, M.D., and Monroe M. Vincent, B.S.N Engl J Med 1980; 303:355-359

August 14, **1980**

## Abstract

Sixty-one patients with leukemia and no immunity to chickenpox were given dialyzable transfer factor or placebo and followed for 12 to 30 months in a double-blind trial designed to examine the clinical efficacy of transfer factor. Sixteen patients in the transfer-factor group and 15 in the placebo group were exposed to varicella zoster, and most of them had a rise in antibody titer. Chickenpox developed in 13 of 15 exposed patients in the placebo group but in only one of 16 in the transfer-factor group ($P = 1.3 \times 10^{-5}$). In the patients treated with transfer factor and exposed to varicella without acquiring chickenpox the titer of antibody to varicella zoster was equal to that in the patients given placebo who became infected with chickenpox. Transfer factor converted negative results on skin tests for varicella zoster to positive in approximately half the recipients. Passive immunization with dialyzable transfer factor appears useful in nonimmune persons. (N Engl J Med. 1980; 303:355–9.)

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We are indebted to D. J. Marmer for technical assistance and to J. Schneider for editorial review.

# Characterization of pBFTM10, a clindamycin-erythromycin resistance transfer factor from Bacteroides fragilis.

**F P Tally, D R Snydman, M J Shimell and M H Malamy**

## ABSTRACT

Bacteroides fragilis TMP10, which is clindamycin-erythromycin resistant (Clnr) and tetracycline resistant (Tetr), contains several plasmids and is capable of transferring drug resistance markers to suitable recipients. We were able to separate a 14.6-kilobase self-transmissible Clnr plasmid, pBFTM10, from the other plasmids of TMP10 in a tetracycline-sensitive recipient strain, B. fragilis TM4000. All Clnr transconjugants acquired an unaltered pBFTM10 and became plasmid donor strains. Transfer is proposed to occur by conjugation since it required to cell-to-cell contact of filter matings and was insensitive to DNase, but sensitive to chloroform treatment of donor cells. The efficiency of transfer of pBFTM10 in a Tets background (TM4003) was not affected by pretreatment of donor cells with clindamycin. A spontaneously occurring Clns derivative, pBFTM10 delta 1, suffered a deletion of DNA, which included a 4.4-kilobase EcoRI fragment. A complex interaction between the autonomous plasmid pBFTM10 and a tetracycline transfer element also present in strain TMP10 was observed since pretreatment of this donor with tetracycline or clindamycin resulted in a marked increase in transfer of both tetracycline and clindamycin resistance.

## Preliminary studies on human "transfer factor" activity in guinea pigs: Systemic transfer of cutaneous delayed-type hypersensitivity to PPD and SKSD

### (ภูมิแพ้แบบช้า)


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- Received 13 November 1975.



- Abstract

More than 50% of primed guinea pigs acquire cutaneous delayed-type hypersensitivity to PPD (purified protein derivative) or SKSD (streptokinase-streptodornase) after injection of antigen-specific human dialyzable transfer factor together with antigen. The ability to respond with delayed-type hypersensitivity does not occur in unprimed animals given transfer factor alone, unprimed animals given transfer factor with antigen, primed animals given transfer factor alone, or primed animals given a second injection of antigen without transfer factor. This system provides preliminary information regarding the action of transfer factor and an animal model for further investigations of transfer factor.


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## Immunotherapy with antibody, lymphocytes and transfer factor in chronic hepatitis B. (ดับอักเสบเรื้อรัง ชนิด B)


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- Received 27 September 1973.



### Abstract

The efficacy of adoptively transferred humoral and cell-mediated immunity in chronic hepatitis B infection was studied in three patients. The first patient with renal failure and chronic active hepatitis received high titered human antibody to the hepatitis B antigen. The second, an asymptomatic chronic antigen carrier, received "immune" lymphocytes and transfer factor (which was not tested for biologic activity in a normal recipient) prepared from the same collection of cells. In the third patient who had acquired hepatitis B from her mother at birth, transfer factor prepared from maternal leukocytes was given on two occasions.

Clinically, there was no change in the first patient's liver function despite transient descreases in hepatitis B antigen and increases in antibody titers. Coexistent antigen and antibody persisted for over 4 mo. In the second patient, the immune lymphocytes induced biochemical signs of transient acute hepatitis associated with increased antigen levels, whereas transfer factor did not have an effect. In the third patient, maternaltransferfactor caused increased hepatitis B antigen and transaminase levels on two occasions. Subsequently, liver function became normal and the antigen titer was reduced by 95%.

Adoptive transfer of humoral immunity does not appear to modify established hepatitis B infection, whereas cell-mediated immunity does. It is postulated that liver cell injury in hepatitis B may be more related to the host's cell-mediated immune response rather than to a cytopathogenic effect of the putative hepatitis B virus.

## Transfer factor in rat coccidiosis

### (โรคบิดในหนู)

### 1972


- E.M. Liburd[2], H.F. Pabst[3], W.D. Armstrong[4]
- University of Alberta, Edmonton, Alberta, Canada. Received **16 June 1972**. Available online 21 October 2004.



# Abstract

An animal model for the evaluation of dialyzable transfer factor (TF) is described. Immunity against the intracellular intestinal protozoal parasite *Eimeria nieschulzi* was transferred to normal rats with TF made from lymphoid tissues of immune rats. *Eimeria* oocyst excretion in the feces was used as a measure of immunity. The reduction of oocyst excretion by animals given TF 48 hr before primary infection was highly significant, when compared with control groups. Animals treated with TF before the primary challenge were completely immune to a second challenge of the parasite. This model may be used to evaluate further the mechanism of TF.


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## Wiskott-Aldrich Syndrome, A Genetically Determined Cellular Immunologic Deficiency: Clinical and Laboratory Responses to Therapy with Transfer Factor*

(ภาวะภูมิคุ้มกันบกพร่องชนิดถ่ายทอดทางพันธุกรรม มีสาเหตุมาจากการกลายพันธุ์ของยีน WAS บนโครโมโซม )


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Communicated by Daniel E. Koshland,


**June 8, 1970**


### Abstract.

Patients with diseases associated with defects in cellular immunity, such as the Wiskott-Aldrich syndrome, characteristically have severe recurrent infections and usually succumb to overwhelming infection at an early age. This communication describes a patient with this syndrome, defective delayed hypersensitivity by skin tests and by in vitro lymphocyte response, who was treated with dialysate of peripheral blood leukocytes (transfer factor). After treatment, the clinical status of the patient improved dramatically, concomitant with the development of delayed hypersensitivity to antigens to which the donor was sensitive. In vitro tests after transfer indicated that the patient's lymphocytes, when stimulated by specific antigen, produced migration inhibitory factor without concomitant DNA synthesis. These observations dissociate skin test sensitivity and activity of migration inhibitory factor from in vitro blastogenesis.
Further, the response to phytohemagglutinin remained diminished before and after therapy. While these findings represent only an individual case, the clinical results suggest that investigation of the use of transfer factor appears warranted in the therapy of Wiskott-Aldrich syndrome and other geneticallydetermined diseases associated with impaired cellular immunity.


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