Transfer Factor and It's Clinical Applications

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The immune system is amazingly complex. Fortunately, nature gives neonates a little help. We are realizing the importance of breast-feeding and immune competency. In this increasingly dangerous world, we are being assaulted by pathogen after pathogen. Our immune systems are faltering. Transfer factor (TF), the premier immune factor in colostrum, can be a vital part of our armamentarium. Transfer factor trains and continually educates the immune system.

H.S. Lawrence discovered transfer factor in 1949, when he demonstrated that an immune fraction of a person's white blood cells was able to transfer immunity in a nonsensitized individual.

Transfer factors are small molecules of 3,500-6,000 kDa molecular weight, consisting of oligoribonucleotides attached to a peptide molecule. In the past, they were derived from dialyzed white blood cells (WBC), but now can be purified from bovine colostrum. They are produced by T-lymphocytes and can transfer the ability to recognize a pathogen to cells that have not been in contact with the pathogen (memory function). They also heighten the immune system's ability to react (increased reactivity or inducer function) to pathogens. Transfer factor probably produces a trigger for T-cell recognition of antigen. On the other hand, it may act as a gene product that assists in antigen presentation to other T-cells.(1)

This inducer fraction of transfer factor links the immune cells with an antigen-binding site, thereby increasing their reactivity to an antigenic stimulus. The suppressor fraction blocks the response of the T-cells,(2) and signals a down regulation of the immune response. This is useful in allergic or autoimmune conditions.

Role of TH1, TH2

Before one can understand the usefulness of transfer factor, it is helpful to have an understanding of the TH1 helper/TH2 helper paradigm. T helper lymphocytes develop along two lines of cell populations. TH1 cells, which modulate cell-mediated immunity, produce the cytokines: IL-2, IFN-gamma, and TNF-alpha. TH2 cells, which modulate humoral immunity, or antibody production, produce IL-4, IL-5, IL-6, IL-10, and IL-13. Once you're familiar with the particular TH1/TH2 predominant phenotypes in a patient, you can more easily identify certain constellations of diseases or conditions, and tailor your therapies.

Cell-mediated or TH1 helper responses are important in the body's ability to defend itself against viruses, fungi, parasites, cancer, and intracellular organisms. Cell-mediated immunity can be tested by:

1. Skin tests–delayed hypersensitivity skin testing;
2. Response to non-specific mitogens, such as phytohemagglutinin (PHA), concavalina, or pokeweed mitogens;
3. Response to specific mitogens, such as diptheria, tetanus, or candida;
4. Response to alloantigens—mixed lymphocyte reaction;
5. T-cell subsets;
6. IL-2R;
7. NK cell level;
8. NK cell activity;
9. IL1 assay; and
10. IL2 and interferon gamma, and other cytokines.

If one has a TH2-dominated condition, with decreased cellular immunity and heightened humoral immunity, the conditions that tend to prevail are:

1. Allergies
2. Chronic sinusitis
3. Atopic eczema
4. Asthma
5. Systemic autoimmune conditions such as lupus erythematosus and mercury-induced autoimmunity
6. Vaccination-induced state
7. Certain cases of autism
8. Hyperinsulinism
9. Pertussis vaccination
10. Malaria
11. Helminth infection
12. Hepatitis C
13. Chronic giardiasis
14. Hypercortisolism
15. Chronic candidiasis
16. Cancer
17. Viral infections
18. Ulcerative colitis

A TH1-dominated picture would include the following medical states:

1. Diabetes type 1
2. Multiple sclerosis
3. Rheumatoid arthritis
4. Uveitis
5. Crohn's disease
6. Hashimoto's disease
7. Sjögren's syndrome
8. Psoriasis
9. Sarcoidosis
10. Chronic Lyme disease
11. H. pylori infections
12. E. histolytica

Pregnancy is a TH2-dominant state. This is an advantage during pregnancy, since a TH1-dominant state, or cell-mediated immune response, would induce rejection of the fetus and placenta.(3) Because it stimulates a TH1 response in most cases, transfer factor should not be used in pregnancy. Certain autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis, which are TH1-dominant states, are ameliorated during pregnancy.(4)

Transfer Factor in Gynecological Conditions	
• ***HPV infections***	• ***Gynecologic cancer***
• ***Chronic vaginitis***	• ***Genital herpes***
• ***Chronic candidiasis***	

TH1-dominant states are generally not helped by transfer factor, and could be exacerbated. Many of them, such as rheumatoid arthritis, multiple sclerosis, and Crohn's disease, are thought to be possibly caused by an infection or reaction to a pathogen. If the TH1 response is an inadequate attempt of the immune system to fight off a microbe, then transfer factor would augment that process and be effective in certain cases. Clinically, this is seen in certain cases, e.g., Crohn's disease, mutiple sclerosis, and chronic Lyme disease, where transfer factor helps a TH1-dominant condition.

Transfer factor augments cell-mediated immunity or pushes a TH2 to a TH1 state. This is useful in TH2-dominated conditions. Normally, on exposure to gut-related microbes and childhood infections, a child's TH2-dominated immune system is subject to TH1 stimulation and TH1/TH2 balance ensues.(5) If TH2 dominance remains, this can lead to atopic, or allergic states. We see this in the increased incidence of allergic symptoms, postnasal drip, asthma, etc., in clinical practice.

The other side of this TH2 state is a decreased TH1 or cell-mediated immunity. With this, we see an increased incidence of viral infection, fungal infection, and cancer. Vaccinations tend to push the immune system toward a TH2-dominant state. To help overcome this tendency, we can use transfer factor pre- and post-immunization.

Cancer, Cell-mediated Immunity, and Transfer Factor

Since cancer can be associated with a TH1-deficient state, use of transfer factor should be considered as part of your therapy of immune augmentation in cancer. Factors that decrease cell-mediated immunity and TH2 dominance are age, cytotoxic cancer treatments, post-surgery stress, metastatic disease, etc.(6) Cell-mediated immunity (CMI) can be a predictor of morbidity and mortality over the age of 60. In patients with liver metastases or colon rectal carcinoma, CMI is predictive of survival.(7) Decrease in cell-mediated immunity, along with an increase in circulating immune complexes, indicates unfavorable prognosis in cancer patients.(8) Studies show that patients who have multiple skin cancers had impaired CMI.(9) In a study of gynecological cancer patients compared to control groups, those on chemotherapy had a decrease in immune perimeters (i.e., refractory decreased cell-mediated immunity), whereas the group getting immunotherapy (in this case, thymopeptin) maintained their immune perimeters at normal levels.(10,11)

Immunologically deficient cancer patients are susceptible to infection by viral pathogens, such as herpes zoster and cytomegalovirus (CMV). Infection occurs as a result of cytotoxic therapy and deficiency of cell-mediated immunity.(12) TH1-dominant states, characterized by increased amounts of IL-2 and IFN-gamma, are immuno-stimulatory and limit tumor growth. In contrast, TH2-predominant patterns, characterized by IL-4 and IL-10 cytokines, are immuno-inhibiting and stimulate tumor growth. HIV progression to HHV8 infection with Kaposi sarcoma, ulcerative colitis, progression to colon cancer, and obesity with increased incidence of carcinoma, are all associated with the increased TH2 state (and decreased cell-mediated immunity). Studies suggest that this shift to TH2 dominance precedes the cancerous transformation. As the cancer grows, it becomes increasingly hypoxic. This leads to further suppression of cell-mediated immunity, allowing decreased immune surveillance. Studies show that a TH2 immune response is associated with a proangiogenesis state, which facilitates cancer growth.(13)

Transfer factor has been shown to improve cellular immunity in patients with immune defects.(14) Since it augments TH1 or cell-mediated immunity, transfer factor is helpful in these situations. For example, by conveying cell-mediated immunity against bladder and prostate tissue-specific antigen, transfer factor was efficacious in the treatment of stage D3 hormone-unresponsive metastatic prostate cancer. Followup showed increased survival rates in 50 patients, with complete remission in two, possible remission in six, and no progression of metastatic disease in (14,15) Transfer factor was shown to improve survival as an adjunct to resection in non-small cell lung carcinoma.(16)

Before transfer factor was derived from colostrum, it was obtained from dialyzed leukocyte extract (DLE). The literature has many citations of DLE of an antigen-specific nature being used for various viral conditions, autoimmune conditions, and certain cancers. It has been found that DLE facilitated immunity to tumor-associated antigen. Fudenburg showed that transfer factor could, from selected donors, increase the cell-mediated responses to tumor-associated antigens in human osteogenic sarcoma patients.

One of the compromises on our cell-mediated immunity is environmental stress (e.g., chemical or heavy metal pollution). It has been shown that long-term exposure to polychlorinated hydrocarbons suppresses phagocytosis, decreases NK cell activity, and reduces lymphocyte response to mitogens in mice.(17) Alterations in immune dysregulation, with a predominantly TH2 response, occurs with lead and mercury exposure. This leads to impaired cell-mediated immunity, increased incidence of infectious disease or cancer, and can end with an autoimmune disease.(18)

Transfer Factor in Allergy and ENT Patients	
• Chronic sinusitis • Chronic allergies • Postnasal drip	• Atopic diseases • Asthma • ENT cancer

Transfer Factor in GI Practice	
• Ulcerative colitis • Viral hepatitis • Chronic candidiasis	• Gastroenteritis • GI cancer

Viral Infections

Currently in medicine, we are seeing increased problems with viral infections, such as otitis media, measles, chronic fatigue, Epstein-Barr virus (EBV), CMV, acquired immunodeficiency syndrome (AIDS), hepatitis, and West Nile virus. We utilize treatment regimens that range from interferon to azidothymidine (AZT), ribavirin, and relenza. However, even with all the high-tech immune weapons available, we are still losing the battle.

In the treatment of viral infections, transfer factor provides a modality that works at a fundamental level. It has been shown to induce interferon in patients with viral infections.(19)

Viral infections tend to have increased TH2 and decreased TH1. This is also seen with fungal infections, parasitic diseases, and cancer. Bacterial infections are associated with decreased TH2-dominant states.

By stimulating TH1, transfer factor may be advantageous in the treatment of hepatitis. In hepatitis C, the activation of the TH2 dominance plays a role in the development of chronic hepatitis changes. TH1 stimulation may result in clearance of viral particles and improvement in the hepatitis.(20,21) Studies show that severe complicated measles has been treated successfully with non-specific transfer factor. Symptoms were ameliorated within 24 hours, without side effects.(22)

One theory claims that one of the mechanisms involved in autistic spectrum disorders is an immune imbalance toward a dominant TH2 pattern, resulting from measles, mumps, and rubella (MMR) vaccination. Currently, a study is ongoing to test the efficacy of transfer factor to act as an immune modulator in this disorder.

It is well-known that viruses play an important role in the etiology of acute otitis media (AOM) in children. In a study of AOM, 75% of the children were positive for viruses such as respiratory syncytial virus (RSV), para influenza, and influenza, and 48% had the causal viruses in the middle ear effusion.(23) These viruses probably act as antecedents to the bacterial infections typical of AOM.(24) This could account for the excellent results seen in early treatment and prevention of otitis media using transfer factor.

A certain percentage of asthmatics have their symptoms precipitated by respiratory infection, most of these secondary to viral infections. A study conducted with transfer factor and

asthmatic patients showed that approximately 50% discontinued their steroid medication and the other half decreased their steroid use. Overall, there was a decrease in hospital admissions. Administration of transfer factor improved cellular immunity. No adverse effects or allergic reactions were observed.(25)

In Annals of Allergy, Kahn reported the increased incidence of infection, such as para influenza virus, syncytial virus, adenovirus, etc., as precipitating factors in children who have asthma. It was also found that children with asthma have a propensity toward frequent infection.(26) Twelve of 15 children exhibited defects in T-cell immunity, many of which were not drastic.(27) This should emphasize that functional, suboptimal defects in cell-mediated immune function can be a factor in viral illnesses, as measured with sensitive immunological testing. Once again, we see that transfer factor can help in conditions with increased susceptibility to viruses, a dominant TH2 (decreased cell-mediated) profile.

It was found that women with extended human papilloma virus (HPV) infections have defective protective mechanisms of cell-mediated immunity.(28) A pronounced shift from TH1 to TH2 cytokine pattern is associated with more extensive HPV infection. Increased gynecological problems are found secondary to HPV. The potential of transfer factor in HPV infections needs to be further explored.

Chronic Infection

The addition of transfer factor can help an impaired immune system that is subject to chronic infections. How many practitioners see this scenario: A child comes down with recurrent bronchitis or tonsillitis, starting shortly after birth, necessitating frequent courses of antibiotics. This can then lead to symptoms of chronic candidiasis. A history of chronic eczema or allergic diathesis can also be found. Immunological or skin testing shows a mild defect in cell-mediated immunity, but no abnormalities. Grohn reported on several similar cases and obtained successful treatment with administration of transfer factor.(29) Here we see that transfer factor is helpful for elevated TH2 states, allergy, chronic candidiasis, and eczema.

Transfer factor has ameliorated cases of recurrent, non-bacterial cystitis (NBRC) when treatment with antibiotics and nonsteroidal drugs was unsuccessful, and cell-mediated immunity to herpes simplex and candida was decreased.(30) Various studies show positive results with transfer factor in chronic mucocutaneous candidiasis.(31)

In Lyme disease, cytotoxic production of a TH2 phenotype is correlated to resistance, while that of a TH1 phenotype is correlated to susceptibility.(32) This suggests that certain people have an immune glitch that makes their immune system prone to either the TH1 or TH2 pattern, and therefore more susceptible to different diseases. This may be precisely where transfer factor, having immune-modulating effects, can be helpful. For instance, in Lyme patients we usually see a TH1- dominated pattern, but transfer factor works very well for certain subsets of Lyme patients.

Chronic Fatigue

Transfer factor has been used in chronic fatigue immune dysfunction syndrome, especially if a viral etiology can be found. It has had varied success, although one may need to use increased dosages. If polyvalent transfer factor is not successful, the use of antigen- (or disease-) specific transfer factor may need to be explored.(33)

In elderly patients with cellular immunodeficiency and chronic fatigue syndrome, age-related decrease in recovery occurred after treatment with transfer factor.34 Success with transfer factor in chronic fatigue syndrome secondary to human herpes virus 6 (HHV6), genital or labial herpes, and recurrent ocular herpes has been well-documented.35-37 A study on the effect of transfer factor on the course of multiple sclerosis showed that it retarded the progression of the disease in mild to moderate cases.(38)

The Treatment

Treatment with transfer factor is dose dependent. In viral infections, one usually starts with three capsules three times a day. The dose is then tapered down to one capsule three times a day. That dose is maintained in cases of chronic viruses, chronic herpes infection, chronic fatigue secondary to CMV or EBV, chronic colds, and impaired resistance. If there is any flare-up in viral infections, the dose can be increased to three capsules three times a day. Usually, patients report decreased susceptibility to colds, decreased nasal symptoms (for instance, postnasal drip and chronic sinus symptoms). In allergic conditions, an adult starts with two capsules three times a day, increasing to three capsules three times a day if symptoms get worse. Again, the dose is tapered to a maintenance level with amelioration of allergic symptoms.

In cases of chronic fatigue syndrome, patients start on three capsules three times a day. One may need to increase the dose depending on the response. Doses of four to five capsules three times daily can be used as an adjunct cancer treatment for patients undergoing chemotherapy and/or radiation therapy, with a resulting decrease in cellular immune function.

Transfer Factor for Immune Disorders
• Cancer • Autoimmune states, e.g., lupus and ulcerative colitis • Chronic fatigue • Fibromyalgia • Lyme disease (certain subsets) • EBV, CMV, HHV6, and other viral infections

Various immune function tests, especially those measuring CMI, can be done to gauge maintenance dosage. One can also perform a cytokine panel, measuring IL-2, IL-4, IFN-U, IL-10, etc. An elevated IL-2 and interferon gamma would indicate a TH1-predominant state, while an elevated IL-4 and IL-10 would point to a TH2-dominated state. NK cell activity, which is usually decreased in cases of cancer, is increased secondary to transfer factor administration, and can be periodically measured.

In pediatric cases with increased susceptibility to viruses, asthma, allergic chronic sinus symptoms, and chronic candida symptoms, initial dosage is:

Under 1 Year: 1/2 capsule a day (200mg of transfer factor per capsule).

1-5 Years: 1/2 capsule a day.

6-12 Years: 1 capsule 2 times a day.

Over 12 Years 1 capsule 3 times a day

These are starting doses; the doses can be gradually increased depending on the severity of the case.

Occasionally, when a patient starts transfer factor, he or she may experience flu-like symptoms, nausea, or gastrointestinal symptoms. Since transfer factor is a small peptide and does not contain milk protein, allergic reactions are rare. These symptoms are usually classified as Jared Herxheimer mechanisms, and they probably signify a direct reaction of transfer factor on gut or systemic pathogens. If patients are informed of these possible mild adverse reactions, they are more likely to continue treatment.

Transfer Factor in Pediatric Practice
• Chronic pharyngitis • Eczema • Allergies • Asthma • Food allergies • Autism (certain subsets) • Prevention of vaccination-induced TH2 states • Chronic infection • Thrush and candidiasis • Otitis media

Transfer Factor for Immune Disorders
• Cancer • Autoimmune states: lupus and ulcerative colitis • Chronic fatigue • Fibromyalgia • Lyme disease (certain subsets) • EBV, CMV, HHV6, and other viral infections

Transfer Factor and Other Alternative Therapies

In complicated immune cases or in adjunct cancer treatment, it is advantageous to add complementary classes of herbs and nutrients to augment the immune-stimulatory effects. These auxiliary factors boost natural killer cell activity, increase phagocytosis, increase maturation of T-cells, enhance general immunity, and trigger the complement cascade, helping cytotoxicity. Compounds that act synergistically with transfer factor include thymic protein factors, Chinese herbs (such as astragalus, cordyceps, shiitake, maitake, and reishi), inositol hexaphosphate, melatonin, 1-3 beta glucan, glutathione, and associated antioxidants. Vitamins A, D, and B6 promote the TH2 pattern, while vitamins E, C, and folate support the production of a TH1 response.(39) Vitamin B12 suppresses the TH1 response.(40) In addition, acupuncture has been found to increase the immune perimeters of CMI. Levels of CD 3+, CD 4+, CD 4+/CD8+, and beta-endorphins were found to be increased in patients with malignant tumors after a course of acupuncture treatment.(41)

Thymic factors cause maturation of naïve T-cells and increase cell-mediated immunity. It is known that transfer factor is more effective in post-thymic cells. Therefore, both thymic factors and transfer factors are recommended for mild thymic primary immunodeficiency.(42,43) A recent study by Dr. D. See showed that transfer factor enhanced natural killer cell cytotoxic activity. The effect of transfer factor was greater than that observed with other well-known NK cell activity enhancers, such as echinacea, acemannan, 1-3 beta glucan, IP-6, and certain Chinese mushrooms. Colostrum had 1/4 the potency. Other immune parameters, such as T-cell function and test of cellular immunity, were not done in this particular study.(44)

Conclusion

Immune system functioning is at the heart of the increasing infectious and immunologic disorders seen in clinical practices. Through its unique properties and activities, transfer factor

is an extremely useful, relatively risk-free alternative and adjunctive therapy for treatment of cell-mediated or TH1-deficient conditions. Think of its potential use in illnesses such as cancer, chronic fatigue, viral infections, allergies, fungal infections, chronic infections, and autoimmune diseases.

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