The Diagnosis and Treatment of CFIDS with Kutapressin

Thomas L. Steinbach MD and William J. Hermann, Jr. MD

After establishing the effectiveness of Kutapressin in 1987, we have treated over 600 patients in a relatively similar fashion with an overall complete or near complete recovery rate of 75%. Our program addresses CFIDS as an "up-regulated" or hyperactive, yet disorganized, immune system caught up in a vicious cycle of producing lymphokines that create the symptoms of fatigue, muscle and joint pain and through variable capillary leakage in the brain, frustrating memory loss and clouded thinking. This immune functional disorganization allows reactivation of resident, dormant viruses including EBV, HHV-6, CMV and, possibly, retroviruses like HTLV II, perpetuating the hyper immune state. Our diagnostic approach attempts to document a disorganized, suppressed T-lymphocyte function. Therapeutically, we use the apparent immune modulating capability of a mixture of small polypeptides called Kutapressin.

The test used to document the immune suppression was developed by Dr. Howard Gratzner at DNA Sciences, Inc. in Houston, in which they made a traditional test, used in transplantation, more precise by adapting it to a flow cytometer. The test is called the SLIF test for Single Lymphocyte Immune Function since the response of each cell to the provoking substance is measured individually. Interpretive guidelines were drawn up using over 250 patients and controls. Testing has been performed on individuals defined by CDC guidelines for CFIDS; no double-blind study has been performed to date. The guidelines have remained effective for over three years, in that, 90% of clinically qualified CFIDS patients are suppressed while 10% are normal. When abnormal, the SLIF is very helpful in monitoring progress toward recovery. Additionally, basic chemistry, hematology, thyroid and autoimmune tests are routinely performed alone with antibody tests to assess viral reactivation. In treating a patient appearing to fulfill the CFIDS criteria, including suppressed immune function, it is essential to continually watch for the emergence of more specific signs indicating other, better defined medical conditions.

When the clinical history and examination indicate CFIDS, the SLIF test shows immune suppression and no other findings indicate a different diagnosis, therapy with Kutapressin is started according to the following protocol:

DNA
SCIENCES, INC
8058 EL RIO
HOUSTON TEXAS 77054
713 748 6800

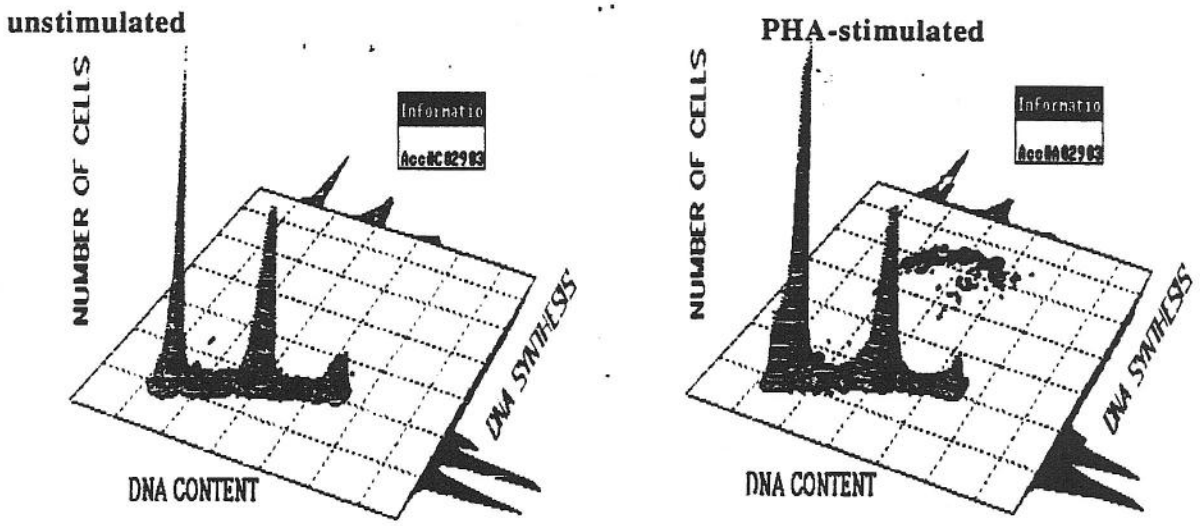
AGE SEX F DRAWN TIME

ADDRESS

REFERRING PHYSICIAN:

BILL TO:

LYMPHOCYTE IMMUNE FUNCTION (LIF)



	SUPPRESSED RESPONSE	
	UNSTIM	PHA
DNA REPLICATION RATE	3.0	310
STIMULATION INDEX	---	103

	NORMAL RESPONSE	
	UNSTIM	PHA
DNA REPLICATION RATE		
STIMULATION INDEX		

The LIF test measures the lectin-induced stimulation of T cell proliferation by flow cytometry. Cells are cultured for 70 hours with PHA, pulsed with iododeoxyuridine and immunostained for DNA replication and DNA content.

12-15-89

HOWARD GRATZNER, PH.D.

DIAGNOSTIC USE OF THE SINGLE LYMPHOCYTE IMMUNE FUNCTION TEST IN CHRONIC FATIGUE SYNDROME

	Primary Illness/ Relapse	Non-CFS (incomplete syndrome)	Healthy Controls
Inhibited	81	7	2
Not Inhibited	12	27	20

Total tests=149

87% Sensitivity of an inhibited test in a clinical CFS patient

91% specificity of a non-inhibited test in the normal population NOT fulfilling CFS criteria

79% specificity of a non-inhibited test in ill patients

90% predictive value of an inhibited result representing CFS

80% predictive value of a normal result representing *absence* of CFS

MONITORING TREATMENT WITH THE SINGLE LYMPHOCYTE IMMUNE FUNCTION TEST

	Poor Response	Good Response
Inhibited	25	17
Not Inhibited	2	37

Total tests=70

93% sensitivity that patient with poor response shows positive/inhibited result

69% specificity that a recovered patient will have normal immune function

95% predictive value that a normal result indicates a recovered patient

60% predictive value that an inhibited result indicates a poor therapeutic response

BACKGROUND AND METHODS

1. Kutapressin™, an injectable liver extract, produced by Schwarz Pharma, Mequon, WI was:

   a. Developed in the 1940's,

   b. Found effective in the 1950's in treating acute allergic reactions of the skin due to its vasoactive, bradykinin inhibiting properties,

   c. Found effective in the 1960's based on anecdotal reports in administer viral illnesses, particularly Herpes zoster ("shingles"),

   d. Noted to be free of significant side effects after nearly fifty (50) years of use.

2. Drs. Steinbach and Hermann reported in CFIDS Chronicle, Spring 1990, on 270 CFS patients, 75% of whom experienced near complete or complete recovery after receiving Kutapressin™ under a standardized protocol.

3. We now report on an additional 130 patients who completed Kutapressin™ therapy under a slightly intensified and elongated protocol from that used in the original study.

Study criteria include:

   a. Patients qualified under modified CDC criteria for CFS,

   b. Therapy for a minimum six (6) months course (approximately 95 injections),

   c. Recovery graded primarily by the patient with physician assistance, on each follow-up visit.

TREATMENT PROTOCOL

Kutapressin™ Therapy for Chronic Fatigue Syndrome Patients of Thomas Steinbach MD and William J, Hermann, Jr. MD

1. Skin test with 0.1cc intradermal Kutapressin™ prior to use,

2. Daily injection of 2cc Kutapressin™ intramuscularly for 25 days,

3. Follow with injections of 2cc Kutapressin™ intramuscularly every other day for 25 injections,

4. Then, injections of 2cc Kutapressin™ intramuscularly given three times per week for a total of six months from the initiation of therapy,

5. SLIF tests are obtained prior to use and during the 3rd and 6th month,

6. Then, if clinical recovery has been achieved and the SLIF test is no longer suppressed, the dose is tapered to two injections per week for the 7th month, one per week for the 8th month, after which therapy is stopped,

7. If a relapse is reported during therapy, a series of 10 consecutive daily injections is given followed by a return to step 3 of this protocol,

8. General instructions to the patients include: adequate rest and attention to a good diet; a multivitamin each day; and moderate exercise, if able, limited to walking or swimming. Total abstinence from alcohol and avoidance of any known "triggers" such as emotional or physical stress, and known allergens are also required.

Kutapressin™ is an old drug with a long safety record and FDA approval (approved for use with skin inflammation only, not CFIDS). The only contraindications are allergy to pork and being pregnant. In our experience, the only rare side effects are limited to local injection site allergic reactions such as itching and bruising. In over 600 patients we have had to stop therapy for acute exacerbation of symptoms in 5 patients. We strongly recommend the intramuscular route since there are much greater problems with subcutaneous injection. This drug is only available through your doctor's prescription. Its cost varies by region and pharmacy but generally is between $70 and $100 per 20cc (10 injection) vial. Insurance reimbursement is variable. Information about the local availability of Kutapressin™ can be obtained from local representatives of the manufacturers, the Schwarz Pharma Kremers Urban Company of Mequon, Wisconsin. Your doctor can contact a Kremers Urban sales representative at (800) 558-5114.

The original, less intensive protocol was published in the CFIDS Chronicle Spring/ Summer 1990 edition. In that study of 270 patients, the referenced 75% response rate is thoroughly analyzed. The above protocol increased the favorable response to 85% and decreased those with no response from 16% to 2%. Collection kits for the SLIF test can be ordered from AMC Immunodiagnostics, Inc. (800) 935-0396.

OUTCOME GRADING BY PATIENT

R_X Failure:

Grade 0- No response

Grade 1- Slight resolution of symptoms

No R_X Significance:

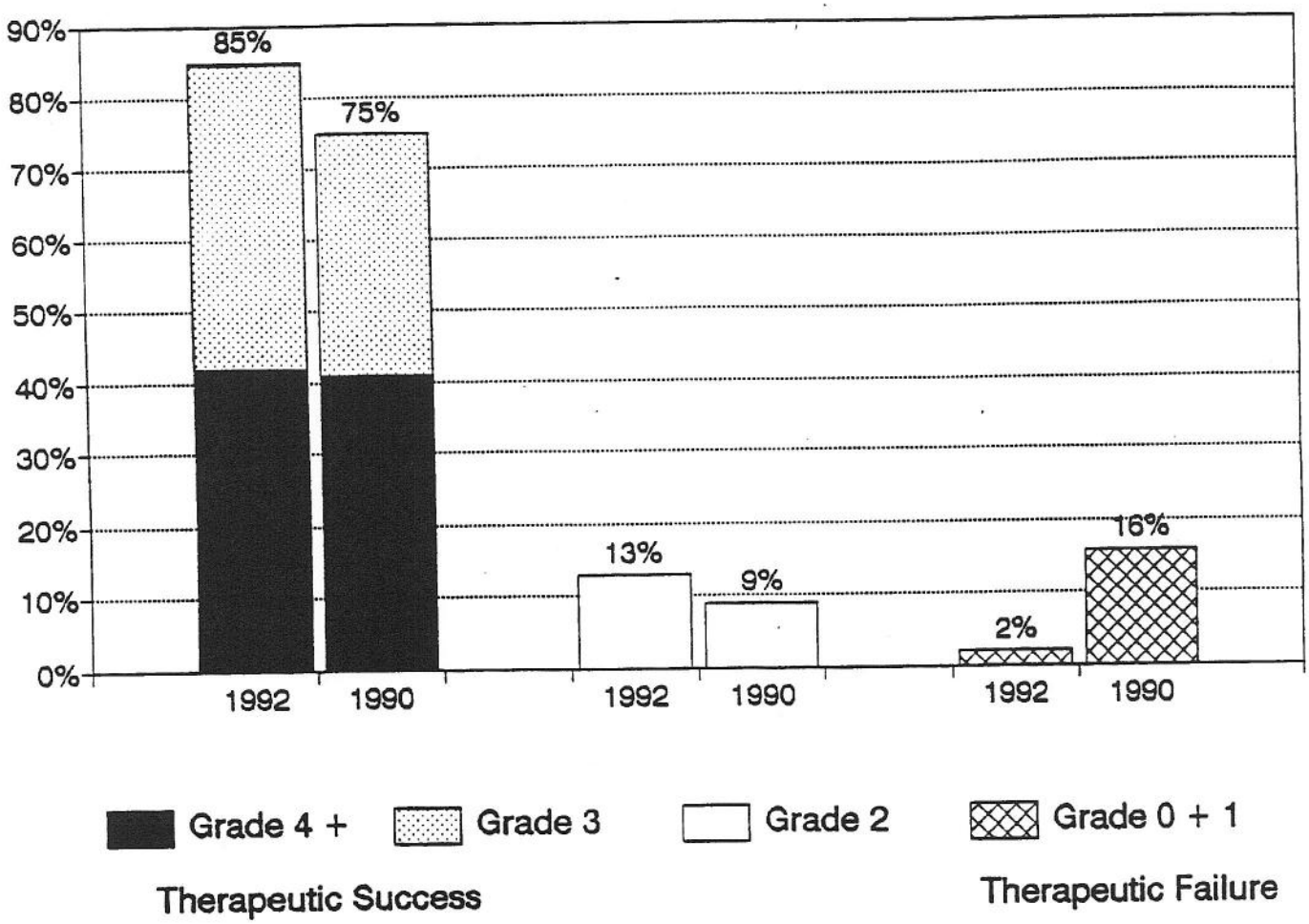
Grade 2- Moderate definitive response with significant symptoms remaining; unable to return to normal activity

R_X Success:

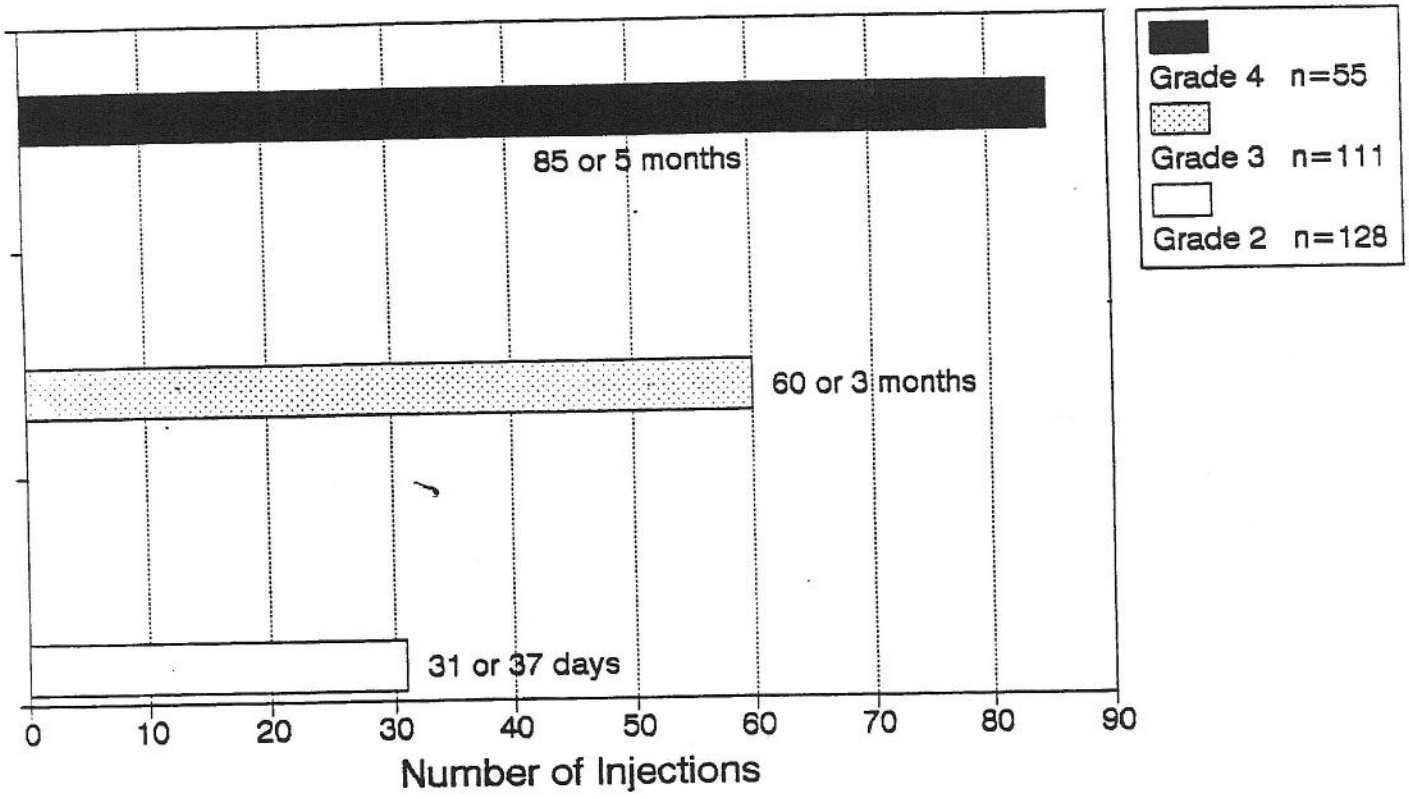
Grade 3- Notable response with return to normal activities and employment, yet few residual symptoms remain

Grade 4- Marked improvement; patient and doctor consider condition resolved

THERAPEUTIC OUTCOME



MEDIAN NUMBER OF INJECTIONS TO REACH GRADE



TIME TO ACHIEVE SUCCESSFUL OUTCOME

	≤ 6 Months	> 6 Months
Grade 4	36 patients	19 patients
Grade 3	59 patients	8 patients

Minor setbacks were experienced by 16% (21 patients) of which twelve (12) eventually reached Grade 3 while four (4) reached Grade 4. Five patients (24% of those experiencing setbacks) failed to achieve a successful therapeutic outcome.

CONCLUSION:

In this study, Kutapressin™ appeared to produce clinical benefit in most CFS patients.

It is imperative to give the therapy adequate time to show progress. We suggest six months minimum if any response is obtained and not discontinuing until fifty (50) injections are reached in cases of no apparent response.