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# MAM14 Immunotherapy New Modality Treat Autoimmune Disorder

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**Abstract**

There is no safe single treatment for autoimmune disorders until this writing. This new modality is challenging this notion with safe no toxic method named MAM14 immunotherapy. This new method have been tried on several types of autoimmune disorders in the last 25 years in our lab at Kuwait University Faculty of Medicine. In this article we demonstrate the difference of MAM14 on four out of the 14 autoimmune disorder studied compared to control who received conventional chemotherapy. Data accumulated of 1400 patients compared to 1400 controls. For the present article the sample we chose 10 patients treated with MAM14 for each disease studied compared to 10 control- patients from the same sickness but treated by conventional immunosuppressant chemotherapy, Cyclosporine, Methotrexate ,Tacrolimus or steroid. MAM14 immunotherapy In brief is vaccination of patients by allogeneic stressed peripheral blood lymphocytes. Peripheral Blood Lymphocytes isolated from venous whole blood on Ficoll-Paque centrifugation.

Cultured for 24 hours in sterile physiological enriched media. Vaccinated subcutaneously into forearm of patients. Vaccination given every 4 weeks for four visits. 4 autoimmune disorder included in this study namely insulin dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis and anterior uveitis. Total 40 patients- treated by MAM14 method 10 patients of each disease compared to 10 control patients of the same disorder but on conventional chemotherapy. Prism Graph pad biostatistical package was used for data analysis. Data accumulated showed significant improvement in signs and symptoms of the present autoimmune disorders studied. Namely insulin dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis and anterior uveitis. MAM14 immunotherapy showed superior improvement and safety on the long run compared to control patients who receive conventional immunosuppressant.

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Mechanism postulated that culturing cells in vitro cause shedding of antigens, these antigens direct autoreactive pathogenic T cells convert to regulatory protective T cells in the presence of peripheral stem cells leading to restoring tolerance and switching off autoimmunity reaction.

***Keywords*:** MAM14 immunotherapy; PBL; IDDM; RA; MS and anterior uveitis; autoreactive T cells; regulatory T cells; Shedding antigens and conventional immunosuppressant's.

## 1. Introduction

There are more than 80 autoimmune disorders [1], however, there is no single safe treatment for autoimmune disorders since corticosteroid era to all current chemotherapy or biotherapy immunosuppressants [2]. Autoimmune diseases occur when the body recognizes its own tissues as foreign and triggers the adaptive immune system to attack them [3].

This reaction may occur in only one organ, such as a joint (as in rheumatoid or psoriatic arthritis), or across multiple organs, as in systemic lupus erythematosus (SLE) [2].Autoimmune diseases can cause physical impairment and a decreased quality of life [3]. Although their exact cause remains unknown, experts suspect a combination of factors, such as genetics and the environment can play a role [1,2,3] .The National Institute of Health estimate that up to 23 million Americans have autoimmune diseases, i e about 8 percent, making them more common than cancer or heart disease [3].These diseases often are marked by periods of remission alternating with incapacitating exacerbations [2]. Because no known cure exists, treatment of autoimmune diseases focuses mainly on managing symptoms and achieving remission [1].

Recommendations include lifestyle modifications, such as regular exercise, a well-balanced diet, plenty of sleep, and stress control. Until recently, pharmacologic treatment was limited to analgesics, nonsteroidal anti-inflammatory drugs (NSAID), and corticosteroids. But since disease-modifying anti rheumatic drugs (DMARDs) were introduced [3]. Many patients have experienced better symptom control and improved quality of life. DMARDs essentially are either chemotherapy or biotherapy medications; many traditionally have been used to treat cancer. Their effectiveness against autoimmune diseases is thought to stem from their immunosuppressant or immunomodulation properties. Both chemotherapy and biotherapy were found up not safe.

You have to assess patients before they enroll in these medication. Before treatment begins, also patient got to give informed consent. In the present revolutionary proposed treatment MAM14 immunotherapy we are uncovering a development which give treatment without the side effect encountered by conventional immunosuppressant's.

In our laboratory at Kuwait university faculty of medicine from 1984-1999. Immunogenetics were employed to look for a mechanism of MAM14 immunotherapy [4,5,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24]. The treatment relied on immune regulation possibly through peripheral blood lymphocyte (PBL) antigen shedding [26], in the presence of peripheral stem cells. regulation possibly through peripheral blood lymphocyte (PBL) antigen shedding [27].

## 2. Methods

Data accumulated of 1400 patients compared to 1400 controls. For the present article the sample we chose 10 patients treated with MAM14 immunotherapy for each disease studied compared to 10 control patients from the same sickness but treated by conventional immunosuppressant chemotherapy : Cyclosporine, Methotrexate , Tacrolimus or steroid.

MAM14 immunotherapy In brief is vaccination of patients by allogeneic stressed peripheral blood lymphocytes (PBL). PBL isolated from venous whole blood on ficoll hypaque centrifugation. Cultured for 24 hours in sterile physiological enriched media. Vaccinated subcutaneously into forearm of experimental- patients only. Vaccination given every 4 weeks for four visits. 4 autoimmune disorder included in this study namely insulin dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis and anterior uveitis. Total 40 treated by MAM14 method 10 patients of each disease compared to 10 control patients of the same disorder but on conventional chemotherapy. Prism Graph pad biostatistician package was used for data analysis.

## 3. Results

Five figures number 1 for INSULIN DEPENDENT DIABETES MELLITUS (IDDM), Figure 2 for RHEUMATOID ARTHRITIS ( RA) , Figure 3 for MULTIPLE SCLEROSIS (MS), and Figures 4 & 5 for ANTERIOR UVEITIS (AU).

A. Insulin Dependent Diabetes Mellitus (IDDM)

Data presented in this article confined to only 4 group of autoimmune disorders out of 14 disorder studied. Consist of 10 IDDM, 10 RA, 10 MS and 10 AU. Total patients presented here, 40 patients treated by MAM14 compared to 40 patients treated by conventional chemotherapy. Figure 1, showed C-peptide significantly increased in IDDM treated by MAM14 immunotherapy compared to control IDDM treated by Cyclosporine.


**Figure 1:** C-PEPTIDE IN 10 IDDM PATIENTS TREATED BY MAM14 IMMUNOTHERAPY COMPARED TO 10 CONTROL IDDM TREATED BY CYCLOSPORINE. P-VALUE < 0.0001 Mann Whitney test.

B. Rheumatoid Arthritis

Figure 2 Rheumatoid Arthritis (RA) showed ESR lowered significantly in 10 RA treated by MAM14 immunotherapy compared to 10 control RA treated by conventional chemotherapy.


**Figure 2:** RHEUMATOID ARTHRITIS ESR MAM14 IMMUNOTHERAPY COMPARED TO CONTROL P-VALUE < 0.0001 Mann Whitney test

C. Multiple Sclerosis

Figure 3 Multiple Sclerosis (MS) showed significant clinical improvement in 10 patients treated by MAM14 immunotherapy compared to 10 control treated by conventional chemotherapy


**Figure 3:** CLINICAL IMPROVEMENT IN MS TREATED WITH MAM14 COMPARED TO CONTROL P VALUE < 0.0055 Mann Whitney test.

**D.** Anterior Uveitis (AU) (Figure 4 and 5)

Figure 4; anterior uveitis showed lymphocyte infiltration examined by, Slit Lamp, reduced significantly in MAM14 immunotherapy treated 10 patients compared to 10 control uveitis treated by steroid eye drops.

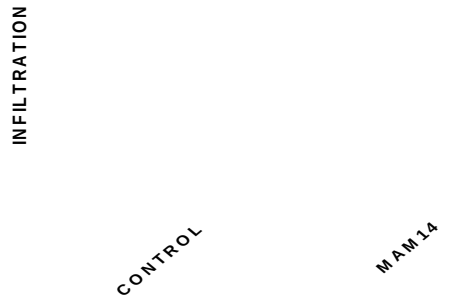


**Figure 4:** anterior uveitis showed lymphocyte infiltration examined by, Slit Lamp, reduced significantly in MAM14 immunotherapy treated patients compared to control uveitis treated by steroid eye drops.

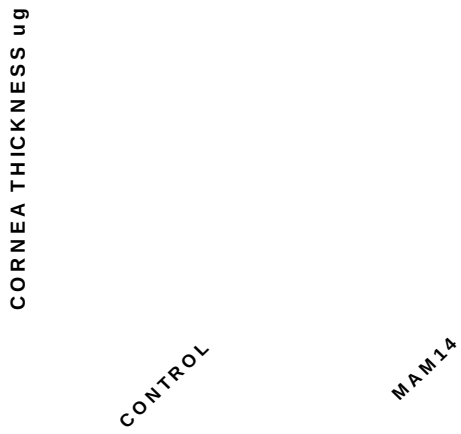


**Figure 5:** ANTERIOR UVEITIS CORNEAL THICKNESS IN 10 PATIENTS TREATED BY MAM14 IMMUNOTHERAPY COMPARED TO 10 CONTROL PATIENTS TREATED BY STEROID EYE DROPS. P VALUE < 0.0001 Mann Whitney test.

## 4. Conclusion

MAM14 CAUSE DRAMATIC SIGNIFICANT IMPROVEMENT IN ALL SIGNS AND SYMPTOMS OF AUTOIMMUNE DISORDERS studied so far [4,5,23,24]. Autoimmune Disorders studied in our laboratory were 14 disorder totaling 1400 patients namely:

IDDM, Rheumatoid Arthritis, SLE, MS , Bronchial Asthm , Uveitis, Allergic Rhinitis , Psoriasis , Rheumatic Arthritis , Alopecia Areata , Autoimmune Thyroiditis, Eczema, pemphigus vulgaris and IgA nephropathy. Results compared to 14 control autoimmune disorder totaling 1400 patients of the same disease but treated by conventional immunosuppressants. Mann Whitney test, used with a two- tailed T test for comparing P values of experiment and control. Data shown in this article are only 4 out of 14 autoimmune disorder namely: IDDM, Rheumatoid Arthritis, Multiple Sclerosis and Anterior Uveitis.

From the graphs presented an examiner notice the superiority of MAM 14 immunotherapy compared to the conventional chemotherapy which is not safe with a limited benefit. Notion of autoreactive T cell conversion to regulatory T cell is well known in immunology practice nowadays [2, 25]. Peripheral Blood Lymphocytes shed antigens when they are stressed in vitro. These antigens play a major role in converting detrimental autoreactive T cells into protective regulatory T cells in the presence of peripheral stem cells leading to switching autoimmunity reaction to tolerance leading to switch off the reaction. This will lead to ameliorating sign and symptom of autoimmunity causing patient relief without the necessity of anti- inflammatory drugs like NSAID or conventional chemotherapy.

The precise mechanism that give rise to autoimmune disease remain incompletely understood [1, 2]. Much of our current knowledge comes from the study of animal models, such as experimental allergic encephalitis and collagen-induced arthritis, in which autoimmunity is induced by direct immunization with self -proteins. These models have taught us much about how tolerance may be broken, but important differences remain between the corresponding animal and human diseases [1]. No cure exist for most autoimmune diseases and treatment is symptomatic [1,2,3]. The available chemotherapy or biotherapy are of limited success and their risk outweigh the benefit [2]. The present MAM14 immunotherapy protocol solves the problem by dealing with converting detrimental autoreactive T cell to protective T regulatory cells [1, 25], by the effect of shedding antigens [26, 27], especially in the presence of peripheral stem cells , restoring in this way self-tolerance which is needed to switch off- autoimmunity reaction.

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