

April 2, 2022
8:30 am - 10:30 am PST



THE MEDIATOR RELEASE TEST (MRT)

*An Advanced and Innovative
Diagnostic Tool Used to Unmask the
Foods that Contribute to your Diet-
Induced Inflammation*

With Dr. Michael A. McLean
Director of Laboratory & Technology
Oxford Biomedical Technologies, Inc
and
Reed Davis, Founder of FDN

BIOGRAPHICAL INFORMATION

High-complexity Clinical
Laboratory Director (ABB)
certification

American Society for Clinical
Pathology (ASCP)
certification

34 years in the study of food
sensitivities and Clinical
Laboratory Operations

Combined 7 years as an
educator serving as an
adjunct professor at Palm
Beach State College and
City College

30 years Research and
Development

Education

- B.Sc. – Biology and Chemistry
- M.Sc. – Dietetics and Nutrition:
Plasma levels of DHEA-s in
Cardiovascular Disease.
- Ph.D. – Dietetics and Nutrition:
Oxidative Stress Biomarkers –
8OHdG and MnSOD



LEARNING OUTCOMES



The Laboratory



Overview of the MRT
Test



Instrumentation – SONY
EC800 Flow cytometer



The Food and chemical
(exogenous and
endogenous) antigens
tested



Quality Control and
Quality Assurance



CLIA MANDATORY REGULATIONS

Laboratory Licensure and Certification

Technologist Certification

Non-regulatory Proficiency Testing

Instrument Calibration

Instrument Maintenance

Technologist Competency Assessment

Technologist Employee Evaluation

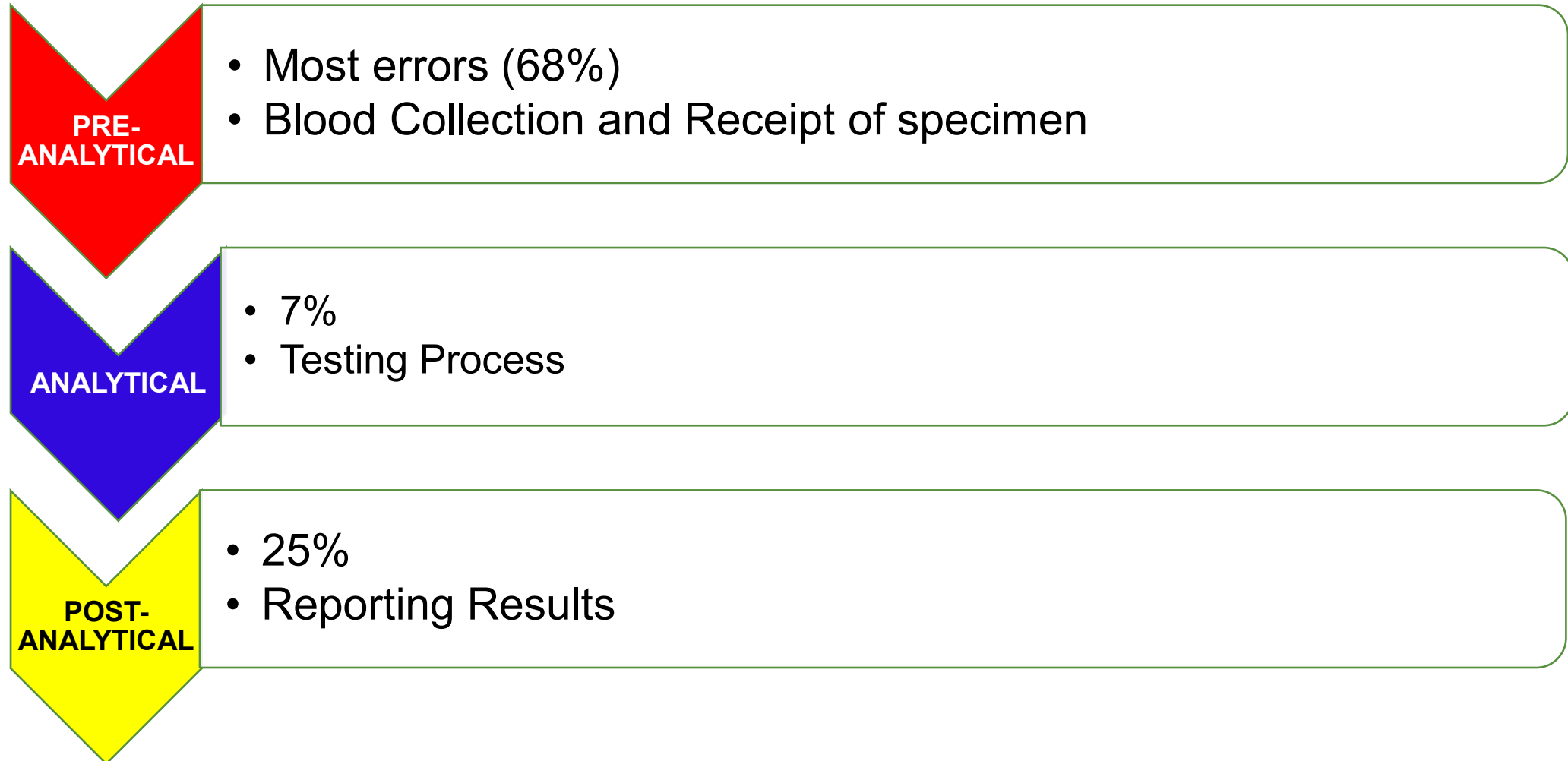
Laboratory - Biennial CLIA Inspection

Technologist - 25 CEUs Biennial

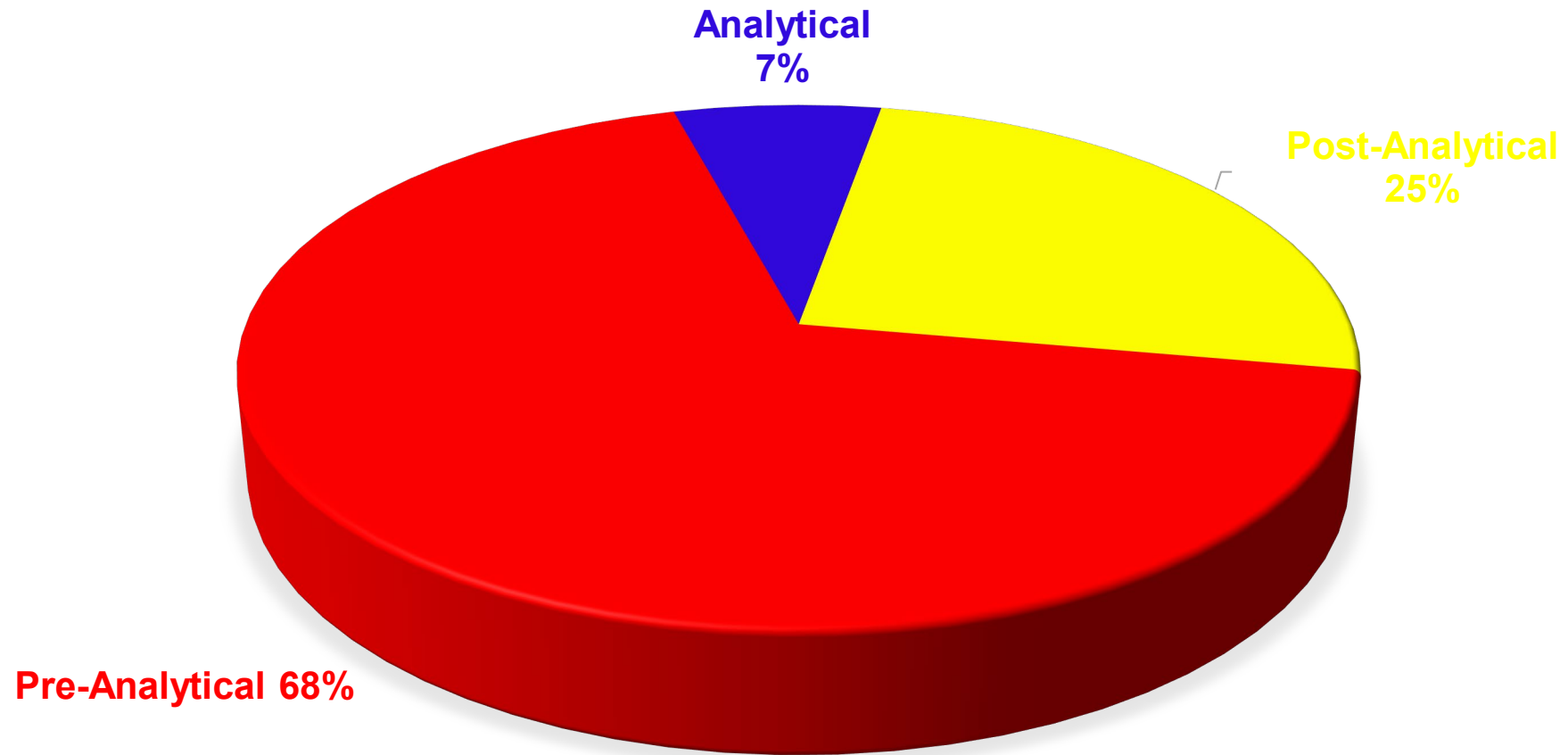


Clinical
Laboratory
Improvement
Amendments

PHASES IN LABORATORY Chain of Custody



ERROR RATES IN LAB PROCESS





OVERVIEW OF THE MRT TEST

- Patient selection or candidate for MRT Test
 - Treatment failures
 - Health and wellbeing
- Patient preparation
 - No preparation before blood draw
- Specimen requirement
 - Standard venipuncture
 - Sodium citrate anticoagulant, 10 – 20 mL whole blood
 - Room temperature, 24-48 hours specimen age
- FedEx overnight courier service



QUALITY CONTROL (QC) AND QUALITY ASSURANCE (QA)

Pre-analytical QC/QA

- Track Shipment
- Specimen Temperature
- Specimen acceptability
 - Appropriate Tubes and Quantity
 - Number of tubes
 - Absence of clots and hemolysis
- Completeness of Requisition form
- Date and Time of Collection
- Patient ID match tube vs. requisition
- Unique Barcode Accession number.
- Specimen Viability



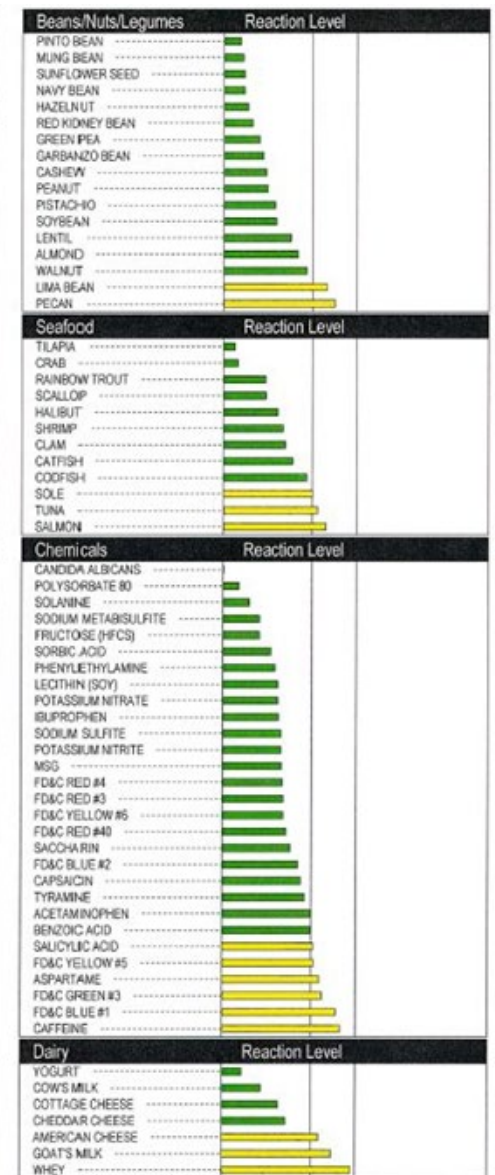
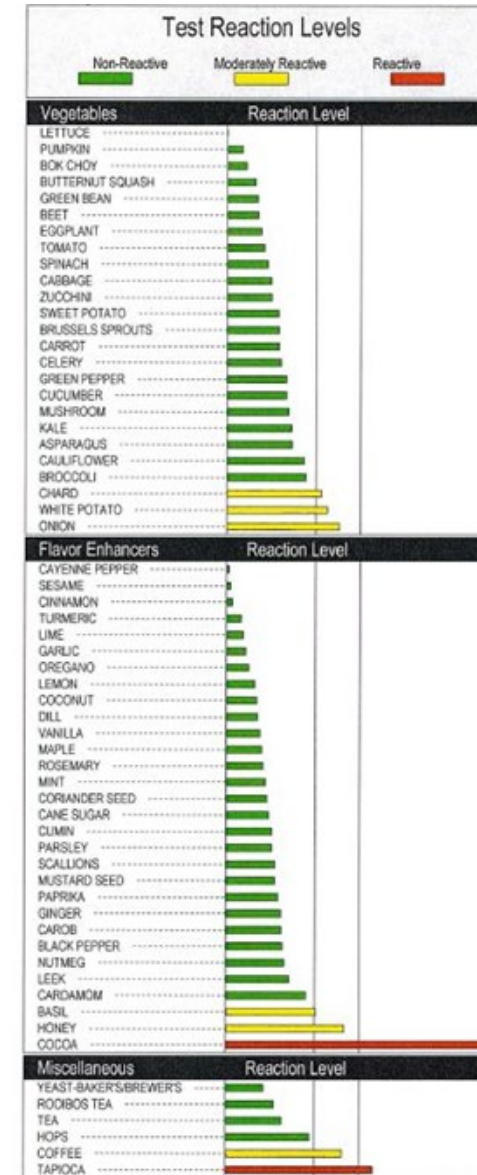
Analytical QC and QA

- Reagent Quality Checks
- Instrument Functionality Checks
- Instrument Calibration Checks
- Patient's Specific Positive/Negative Quality Control Checks
- Visual and Automated Data Reduction Checks



Post-analytical QC and QA

- Data Reduction
- Printed Results
- Correct Patient's Name
- Correct Client
- Ship – Tracking Number





THE IMMUNE SYSTEM AND OUR UNIQUE APPROACH

FOUR TYPES OF HYPERSENSITIVITY

Innate and Adaptive


- **Type 1** – IgE Mediated (Anaphylactic), i.e., peanut allergy
- **Type 2** – Antibody dependent (complement activation), i.e., AHA
- **Type 3** – Immune Complexes, i.e., SLE, RA
- **Type 4** – Delayed Cell-mediated, i.e., TB, GVHD

IMPORTANT NOTE: MRT IDENTIFIES THE FINAL COMMON PATHWAY FOR NON-IgE DEPENDENT MECHANISM OF DIETARY PROTEINS CHALLENGES.

Inflammation Biomarkers in blood

Interleukins or Cytokines

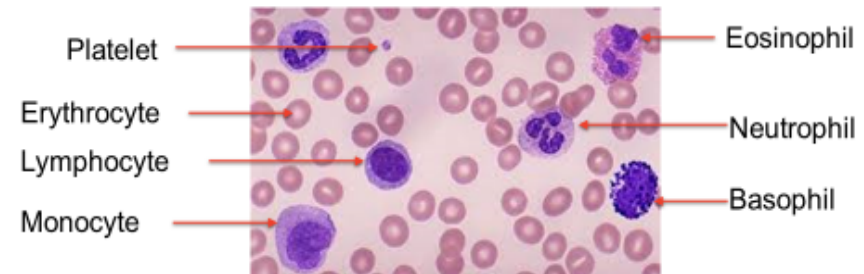
- Neutrophils
 - IL1- β , IL-6, IL-8, TNF- α
- Monocytes
 - IL1- β , IL-6, IL-8, TNF- α
- Lymphocytes (T-cells, B-cells)
 - IL-6
 - TNF- α



INSTRUMENTATION USED IN HEMATOLOGY

Brightfield Microscopy

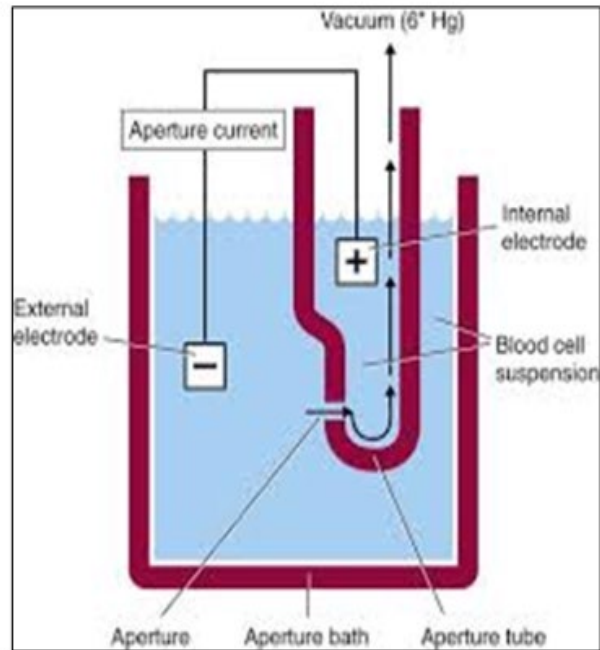
BLOOD FILM 100X BRIGHTFIELD MICROSCOPE



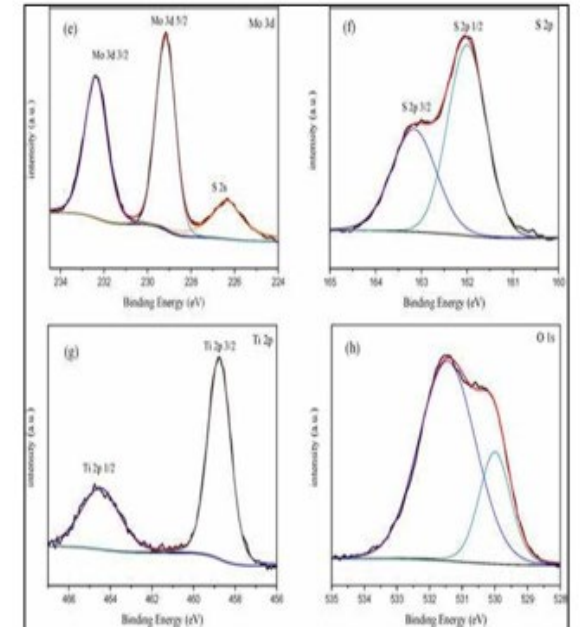
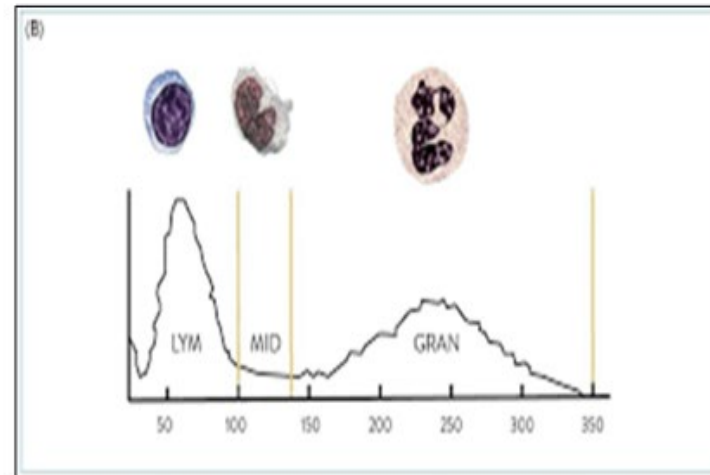
<https://www.drcroes.com>

Resistivity and Impedance Technology

ELECTRICAL IMPEDANCE

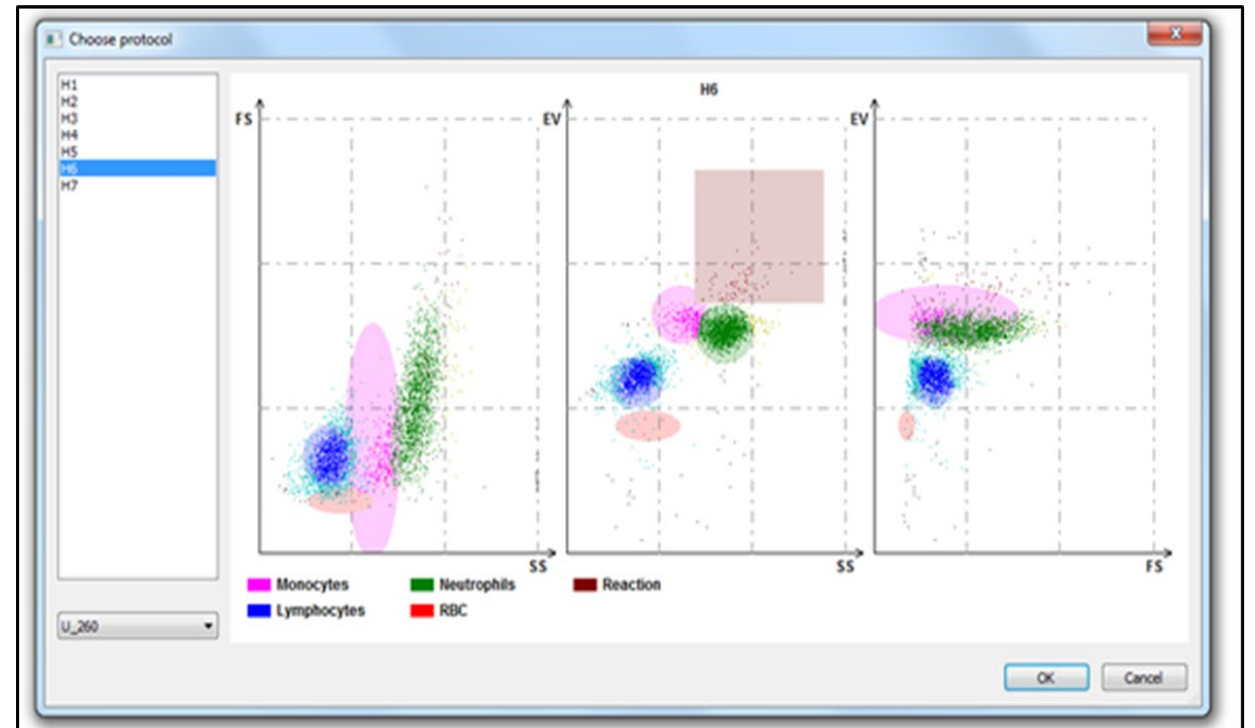
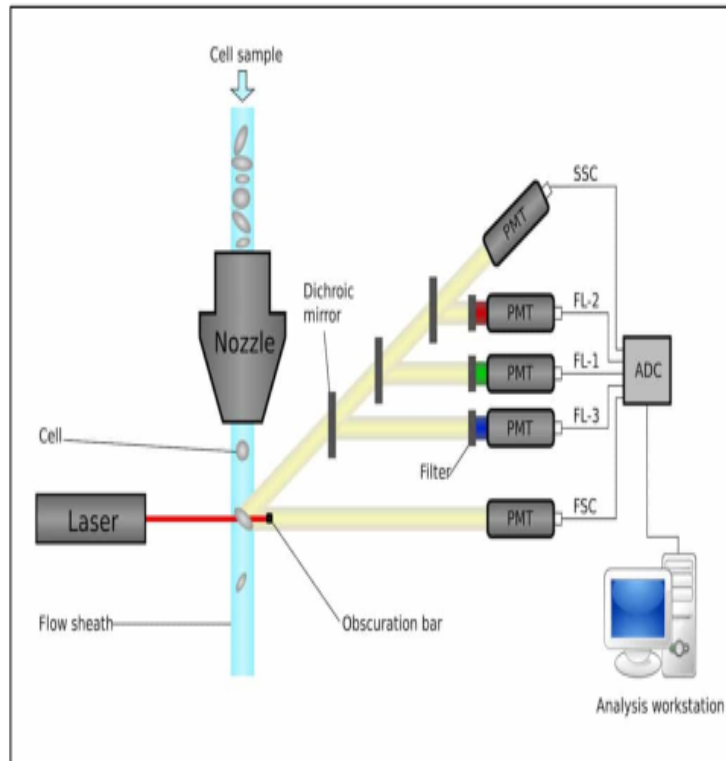


HISTOGRAM



LASER TECHNOLOGY

HYDRODYNAMIC FOCUSING



FLOWCYTOMETRY INSTRUMENTATION



SONY EC800 DUAL METHOD



BIORAD BIOPLEX 200 SYSTEM

What's the last piece of the puzzle that was not cover but is very important?





ANTIGENIC STIMULI

Food Antigen Quality: Exceptional and Stringent QC

- Standardized raw materials ensure a consistently high quality of allergen extracts
- Optimized extraction method based on in-house research and development guarantee high quality.
- Validated production processes ensure batches with reproducible quality
- EN ISO 13485 certified
- Quality certificate with protein content and concentration show the quality of the allergen extracts – SDS Page of extract silver stained.
- Long shelf life up to 10 years at -20°C (-4°F)

RESULTS FROM THE MRT TEST

- INDIVIDUALIZED
- MORE THAN 2000 CELLS ARE COUNTED AND CHARACTERIZED FOR EACH ANTIGEN
- REACTIVITY OF SPECIFIC ANTIGEN EVALUATED AGAINST THE PATIENT'S OWN BASELINE
- REACTIVITY DETERMINED VIA A SOPHISTICATED ALGORITHM AND DATA REDUCTION SOFTWARE.
- FINALLY, THE INTERPRETATION OF THE DEGREE OF REACTIVITY IS PROVIDED BY THE RESULTING SOFTWARE AND PRESENTED IN AN EASY TO UNDERSTAND FORMAT.

INTERPRETATION

SDI	REACTIVITY	CODE
≤ 1.99	Non-reactive	GREEN
2.00 – 2.99	Moderate	YELLOW
≥ 3.00	High	RED



CLINICAL UTILITY

Clinical Indications for Mediator Release Test (MRT)

- Non-IgE mediated foods is often an important symptoms-provoking stimuli for many GI disease and other food sensitivity related disorders.
- Early intervention is key...it allows early intervention by healthcare practitioner, thereby maximizing outcomes.
- Food sensitivities may be a trigger for migraine, fibromyalgia, Irritable Bowel Syndrome, Inflammatory Bowel Disease, autoimmune disease, GERD, Joint Pains, Skin eruptions, ADD, and weight imbalances.

Clinical Indications For Mediator Release Testing (MRT®)



Non-IgE mediated food and food-chemical hypersensitivity can be an important symptom provoking component in D-IBS, migraine, fibromyalgia, and other food sensitivity related disorders. Appropriate early intervention will enable physicians to more quickly maximize outcomes in their food sensitive patients. The charts below list clinical parameters that when present, either increase or decrease the likelihood that hypersensitivity reactions play a role in the etiology of the patient's condition.

Suspect Non-IgE Food Hypersensitivity When:

- ◆ Symptoms are chronic and frequent
- ◆ Many co-morbidities
- ◆ Evidence of mediator release (active inflammatory process)
- ◆ Excess mucus production (Hx of IgE allergy)

Migraine

Increased Probability

- ① Chronic & frequent >2x per month
- ① Frequent headaches in between episodes
- ① Personal or family Hx of IgE mediated allergy
- ① Hx of adverse food reactions
- ① Other target indications or secondary indications are co-morbid
- ① Resistant to relief from medication

Decreased Probability

- ① Infrequent (<1x per month)
- ① Hormonally induced
- ① Weather induced
- ① Trauma induced

Fibromyalgia

Increased Probability

- ① Co-morbid diarrhea
- ① Personal or family Hx of IgE mediated allergy
- ① Hx of adverse food reactions
- ① Other target indications or secondary indications are co-morbid
- ① Resistant to relief from medication

Decreased Probability

- ① Diarrhea not present
- ① Co-morbid constipation (Unless constipation is due to side effect of medication)

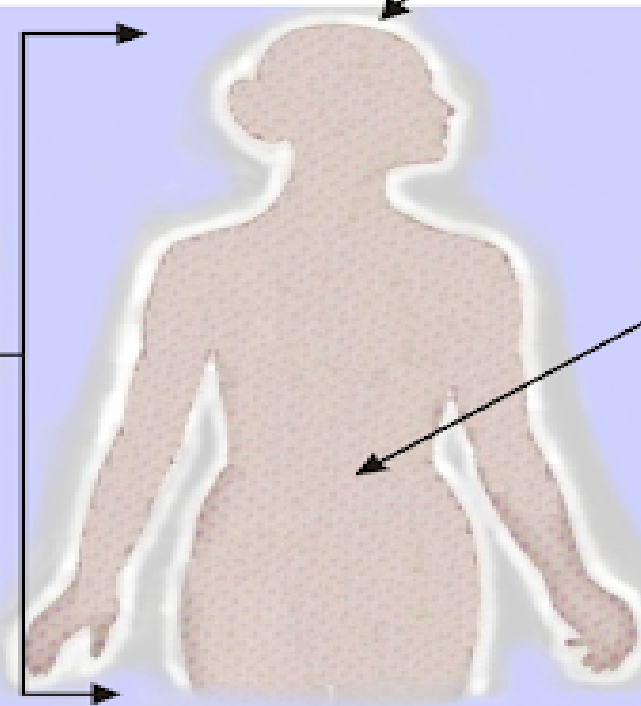
Irritable Bowel Syndrome

Increased Probability

- ① Diarrhea component (either D-predominant or cyclic)
- ① Chronic & frequent
- ① Refractory
- ① Personal or family Hx of IgE mediated allergy
- ① Hx of adverse food reactions
- ① Other target indications or secondary indications are co-morbid

Decreased Probability

- ① Constipation predominant
- ① Infrequent attacks (< 2x/month)



Clinical Utility

Secondary Indications & Common Co-Morbidities

- Functional Diarrhea
- Dyspepsia
- Recurrent Secondary Headaches
- Celiac Sprue
- Cyclic Vomiting Syndrome
- Inflammatory Bowel Disease
- Chronic Sinusitis
- Non-Seasonal Rhinitis
- Chronic Sinus Headaches
- Chronic Otitis Media w/effusion
- Chronic Urticaria
- Eczema
- Autism Spectrum Disorders
- Attention Deficit Disorder
- Hyperactivity with or w/o A.D.D.
- Arthralgia
- Rheumatoid Arthritis
- Chronic Fatigue Syndrome

LIFESTYLE EATING AND PERFORMANCE LEAP

- Uses the results of the MRT Test
- It is a personalized dietary approach based upon the proven principles of oligoantigenic diets
- It is implemented by eliminating moderate to high –immune-reactive tested items.
- The eating plan includes only those foods and ingredients tested by the MRT method.
- Three (3) phase approach, each phase ranges from 4-6 weeks.
- The goal of the LEAP eating plan is to reduce or eliminate the level of adverse reaction and ultimately symptoms.
- Improve quality of life (QOL)

LEAP – DIETARY MANAGEMENT TOOL

PHASE 1

- 10-30 DAYS IN DURATION
- SAFE ITEMS (GREEN CATEGORY)
- THE GOAL IS TO REDUCE INFLAMMATION AND SYMPTOMS

PHASE 2

- 20-30 DAYS IN DURATION
- TEST UNSAFE FOODS ORAL CHALLENGE
- THE GOAL: ADD MORE SAFE FOODS

PHASE 3

- 30-60 DAYS IN DURATION
- ORAL CHALLENGE WITH UNTESTED FOODS
- THE GOAL: VARIETY, ADDITIONAL FOODS

PEER-REVIEWED MANUSCRIPTS

1. Kaczmariski M, Pasula M, Sawicka E, Werpachowska I. MRT test - New generation of tests for food hypersensitivity in children and adults. Przegląd Pediatriczny. 1997(SUPLEMENT 1):61-65. <http://dietetykametaboliczna.com/publikacje/>
2. Pasula MJ, Nowak J. Particle size measurement in suspensions: Part 1--A laboratory method for exploring food allergies and sensitivities in illness. Am Clin Lab. 1999;18(4):16-18. <https://pubmed.ncbi.nlm.nih.gov/10539096/>
3. Pasula MJ. Particle size measurement in suspensions. Part 2: An in vitro procedure for screening adverse reactions to foods and chemicals. Am Clin Lab. 1999;18(9):14-15. <https://pubmed.ncbi.nlm.nih.gov/10623324/>
4. Zarini GG, Masters J, McLean MA, Strobel CT. Clinical and Anthropometric Improvements with a tailored Dietary Approach in Pediatric Crohn's Disease. Altern Ther Health Med. 2021 Mar 13:AT6717. <https://pubmed.ncbi.nlm.nih.gov/33711815/>

PUBLISHED ABSTRACTS

1. Patenaude J & Bright D. Clinical improvement of IBS, migraine, fibromyalgia and arthritis using elimination diets based on mediator release blood testing. Journal of the American Dietetic Association, Volume 109, Issue 9, Supplement, 2009, Page A32, ISSN 0002-8223, <https://doi.org/10.1016/j.jada.2009.06.092>.
(<http://www.sciencedirect.com/science/article/pii/S0002822309008645>).
2. Williams F. Use of the LEAP mediator release test to identify non-IgE mediated immunologic food reactions that trigger diarrhea predominant IBS symptoms results in marked improvement of symptoms through use of an elimination diet. American Journal of Gastroenterology: October 2004 - Volume 99 - Issue - P S277-S278.
(https://journals.lww.com/ajg/Fulltext/2004/10001/USE_OF_THE_LEAP_MEDIATOR_RELEASE_TEST_TO_IDENTIFY.847.aspx).

MAGAZINE PUBLICATIONS

1. Patenaude J. Behavioral Nutrition Health Roundtable. Obesity in the age of weight neutrality: How are registered dietitian nutritionists responding to the challenge? Academy of Nutrition and Dietetics. BHNewsletter, Spring 2020, Volume 37 No. 1, Page 5. https://www.bhndpg.org/wp-content/uploads/2020/07/BHNews-Spring2020_FINAL-2.pdf
2. Patenaude J. Inflammation and food sensitivities — successful treatment begins with patient-centered care. Today's Dietitian, November 2011 Issue; Vol. 13 No. 11 P. 18. <https://www.todaysdietitian.com/newarchives/110211p18.shtml>
3. Alternative approach to IBS and migraine is winning over providers. Dis Manag Advis. 2004;10(1):6-1. <https://pubmed.ncbi.nlm.nih.gov/15007999/>

PUBLICATIONS IN PROGRESS/ PREPARATION

1. Zarini GG, Masters J, McLean MA, Strobel CT. Clinical and anthropometric improvements with a tailored dietary approach for pediatric Crohn's disease. Pediatric Health, Medicine and Therapeutics, 2020. Under review.
2. Braunstein N, Hogan M, Diaz R. The Lifestyle Eating and Performance (LEAP) program for improving quality of life in women with PCOS: A pilot study of dietitian-directed therapy. In preparation.
3. Zarini GG, McLean MA. Tailored oligoantigenic based dietary approach for migraine. In preparation.

RESEARCH STUDIES IN DEVELOPMENTAL STAGE - 2021

- **Prospective IBS Study**– Effectiveness of the LEAP program for the treatment of Irritable Bowel Syndrome (IBS).

Outcomes:

- Plasma cytokine levels
 - IBS symptomatology
 - Quality of life
- **Prospective plasma inflammatory biomarkers in disease management**
 - **Population studies in loss of oral tolerance in multiple diagnosed disease**



Title: Tailored Dietary Approach to Manage Irritable Bowel Syndrome

Susan Linke, MBA MS RDN LD CLT, Jan Patenaude, RDN CLT, Gustavo Zarini, PhD RD & Michael McLean PhD

Background: Irritable Bowel Syndrome (IBS) is more prevalent in women than men, and IBS symptoms negatively affect their Quality of Life (QoL).

Objective: We investigated the effectiveness of a tailored dietary approach to managing IBS symptomatology and QoL among women.

Methods: The retrospective study included women (n=21) with a physician diagnosis of IBS. Blood was collected, and the Leukocyte Activation Assay-MRT (LAA-MRT) was performed using Flow Cytometry Systems by Oxford Biomedical Technologies, Inc. White blood cells reactivity was analyzed using a LAA-MRT software to scale the degree of an adverse immune response to 150 food and food-chemical antigens. The Lifestyle Eating and Performance (LEAP) program is an oligoantigenic dietary approach based on the LAA-MRT results, which was administered by a dietitian. A symptom survey was used to evaluate the severity and frequency of gastrointestinal (GI) symptoms and were quantified from a scale of 0 (low) - 4 (high) with a possible score of 0 to 36. Quality of life was measured by the Short Form-36 (SF-36) Health Survey. Scores from the eight SF-36 domains range from 0 to 100, with a greater score signifying a more desirable health state. Institutional Review Board (IRB) approval was received to conduct research.

Results: The patients' mean age was 42.6 years and had a BMI of 25.8 kg/m². Mean follow-up time from the first to the second visit was 19.9 days. Adjusted linear mixed models showed a significant reduction in GI symptoms associated with IBS (16.6 vs. 6.7, P<0.001) and increase in QoL [physical functioning (81.1 vs. 90.6, P=0.003), role physical (27.0 vs. 78.3, P<0.001), vitality (30.2 vs. 57.9, P<0.001), bodily pain (47.4 vs. 73.1, P=0.003), and emotional well-being (61.6 vs. 77.8, P=0.003).

Conclusion: Findings from the study support using the LEAP program as an adjunctive treatment option for women with IBS. Tailored dietary approaches are needed to advance the care of IBS patients.

BACKGROUND

- Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder described by abdominal discomfort or pain and abnormal bowel habits.
- IBS is more prevalent in women than men, and IBS symptoms negatively affect their Quality of Life (QoL).
- The pathophysiology of IBS is multifactorial and is not entirely understood.
- Foods and dietary behaviors could influence the generation of symptoms associated with IBS.
- Several IBS diets with different rationale and results have been previously investigated. However, there is a lack of studies examining tailored dietary approaches for the treatment of IBS.

OBJECTIVE

- We investigated the effectiveness of a tailored dietary approach to managing IBS symptomatology and QoL among women.

METHODS

- The retrospective study included women (n=21) with a physician diagnosis of IBS.

METHODS (cont'd)

- A symptom survey was used to evaluate the severity and frequency of gastrointestinal symptoms and were quantified from a scale of 0 – 4 with a possible score of 0 to 36 points.
- Quality of life was measured by the Short Form-36 (SF-36) Health Survey. Scores from the eight SF-36 domains range from 0 to 100, with a greater score signifying a more desirable health state.
- Institutional Review Board (IRB) approval was received to conduct research.
- Statistical analysis was performed using SPSS version 25 and significance was set at $P < 0.05$.

RESULTS

- The patients' mean age was 42.6 years and had a BMI of 25.8 kg/m². Mean follow-up time from the first to the second visit was 19.9 days (Table 1).
- Adjusted linear mixed models showed a significant reduction in gastrointestinal symptoms associated with IBS (16.6 vs. 6.7, $P < 0.001$) and increase in QoL [physical functioning (81.1 vs. 90.6, $P = 0.003$), role physical (27.0 vs. 78.3, $P < 0.001$), vitality (30.2 vs. 57.9, $P < 0.001$), bodily pain (47.4 vs. 73.1, $P = 0.003$), and emotional well-being (61.6 vs. 77.8, $P = 0.003$).

Table 2. Measures Pre- and Post-Dietary Intervention

	Pre-LEAP program M (SE)	Post-LEAP program M (SE)
Gastrointestinal Symptom Survey Score	16.6 (1.8)	6.7 (1.0)
SF-36 Health Survey		
Physical functioning	81.1 (5.1)	90.6 (3.5)
Role physical	27.0 (8.2)	78.3 (9.1)
Role emotional	57.6 (11.8)	73.4 (11.7)
Vitality	30.2 (6.8)	57.9 (6.1)
Bodily pain	47.4 (4.8)	73.1 (5.2)
Social functioning	53.7 (7.9)	67.1 (6.1)
Emotional well-being	61.6 (5.3)	77.8 (3.4)
General health	50.2 (7.1)	61.2 (11.1)

CONCLUSION

- IBS clinical manifestations present significant challenges in managing IBS. A tailored dietary intervention plan an adequate dietary intervention.

POSTER PRESENTATIONS/ CONFERENCES 2021



American Society for Nutrition
Excellence in Nutrition Research and Practice
www.nutrition.org



Where the **Best** in Science & Health **Meet**
June 7-10, 2021

WEBSITE

Updated –▶

**Oxford Biomedical
Technologies, Inc. Website**

<https://www.nowleap.com/>

Updated –▶

Research Page

<https://www.nowleap.com/research/>

Thank You!

