Biocidin Botanicals®

Metabolic Syndrome/Insulin Resistance Protocol

Introduction

Metabolic Syndrome (MetS) is a cluster of conditions that raise the risk of serious illness. Left untreated, MetS can progress to disorders such as Type 2 diabetes and non-alcoholic fatty liver disease.[1] Additionally, MetS is strongly associated with developing atherosclerotic cardiovascular disease (CVD), increasing the risk of coronary artery disease and stroke.[2] It has gained much attention in the last decade due to its dramatic increase worldwide.

Epidemiology

MetS is about three times more common than diabetes, and the global prevalence can be estimated at one-quarter of the world population. In other words, over a billion people in the world experience metabolic syndrome.[3] The most accepted hypothesis for developing MetS is insulin resistance. In fact, it is often referred to as insulin resistance syndrome.

Diagnosis

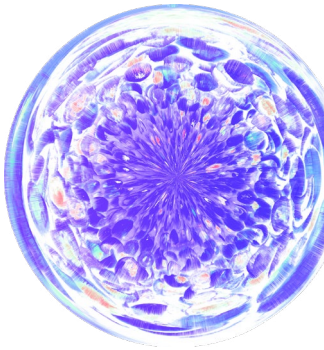
Currently, the widely accepted definition of MetS comes from the World Health Organization. It states that the following criteria must be met for a diagnosis:

- Presence of insulin resistance
- At least two of the following:
    - Elevated fasting blood glucose (often present with insulin resistance)
    - Elevated blood triglycerides
    - Low HDL cholesterol
    - Elevated blood pressure
    - Abdominal adiposity (aka central obesity or large waistline)

Risk Factors

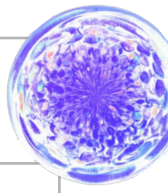
The following factors increase the chances of having metabolic syndrome:[4]

- Age
- Ethnicity. Hispanics – especially Hispanic women – appear to be at the greatest risk of developing MetS
- Sedentary lifestyle
- Obesity. Visceral adiposity is a primary trigger for most of the pathways involved in MetS[5]
- Diabetes. MetS is more likely following gestational diabetes or if there is a family history of Type 2 diabetes
- Non-alcoholic fatty liver disease
- Polycystic ovary syndrome
- Sleep apnea



Metabolic Syndrome and the Microbiome

Both genetic and environmental factors play a role in the development of MetS. Dysbiosis (both gastrointestinal and oral) is an important modifier in each of these categories. The table below lists the fundamental physiological changes associated with MetS.



Central players in the initiation, progression, and transition of MetS to CVD.[6]	**Relationship to the Microbiome**
Insulin resistance	Dysbiosis results in intestinal permeability, increasing the absorption of lipopolysaccharide (LPS), leading to increased activation of inflammatory pathways, and impairment of insulin signaling, with decreased phosphorylation of the insulin receptor.[7]
Neurohormonal activation	• Gut microbiota can either activate or inhibit the HPA axis. • SCFAs are crucial for the maturation and function of microglia, the resident macrophages of the central nervous system. • An imbalance of the gut microbial community (induced by stress or diet) can lead to inflammatory processes and activation of the HPA axis. • Under conditions of a missing or dysbiotic microbiota, especially early in life, the brain's high metabolic demand may be insufficiently met due to nutrient deficiencies. This insufficiency is known to contribute to long-term neuroendocrine disturbances[8]
Chronic inflammation	• The gut microbiota and its metabolites may regulate host inflammatory conditions. • Numerous studies have linked the gut microbiota to inflammatory diseases such as Crohn's disease, ulcerative colitis, multiple sclerosis, and rheumatoid arthritis (RA). • The gut microbiota plays a role in the pathogenesis of inflammatory diseases such as asthma, Type 1 and Type 2 diabetes, and obesity.[9]

Metabolic Syndrome and the Microbiome (continued)

Research shows a significant connection between a balanced microbiome and healthy metabolic function – including the prevention and possible treatment of MetS and insulin resistance.[10] Specific strains of bacteria play a role in immune and metabolic signaling and maintaining gut barrier integrity. Endotoxins producing gram-negative bacteria need to be kept in check while simultaneously maintaining increased diversity in favorable strains to create a healthy microbiome.

Bacterial LPS activation of toll-like receptors leads to innate immune responses that impair insulin sensitivity. Additionally, LPS, TMA, and other inflammatory metabolites then enter systemic circulation, where they upregulate inflammation through TLR-4 receptor activation. The result is chronic inflammation in the liver and adipose tissue that is associated with the development of IR, CVD, and other conditions seen in MetS.[11]

The beneficial impact of a healthy diet on MetS is due in part to its effect on microbial balance in the GI tract. For example, a high-fat, low-fiber diet induces intestinal dysbiosis, which results in a disruption of tight junction integrity. Conversely, high-fiber diets support a more diverse and robust microbiome.

Fiber fermentation plays a significant role in supporting the integrity of the gut lining. Metabolites produced by microbial fermentation of fibers induce the production of the endogenous peptides known to have beneficial effects on glucose metabolism and to improve intestinal epithelial tight junction integrity (GLP-1 and GLP-2).[12]

There has been a recent trend in the use of glucagon-like peptide-1 (GLP-1) receptor agonist medications to support weight management and appetite control. These act to mimic GLP-1, which is an incretin and satiety hormone that is released from L-cells in the gastrointestinal tract in response to eating. GLP-1 causes the body to produce more insulin, which reduces blood glucose (sugar) and suppresses appetite, thereby supporting energy balance, glucose homeostasis, and body weight control.

Through fermentation of non-digestible starches and prebiotic fibers, the microbiome produces a range of metabolites, including secondary bile acids and short-chain fatty acids (butyrate, propionate, acetate, etc.), which have been shown to stimulate GLP-1 secretion.[13] This represents an important crosstalk pathway between gut microbes and host cells via enteroendocrine peptides. This crosstalk can be supported through dietary intervention and microbiome modification for an integrative approach.

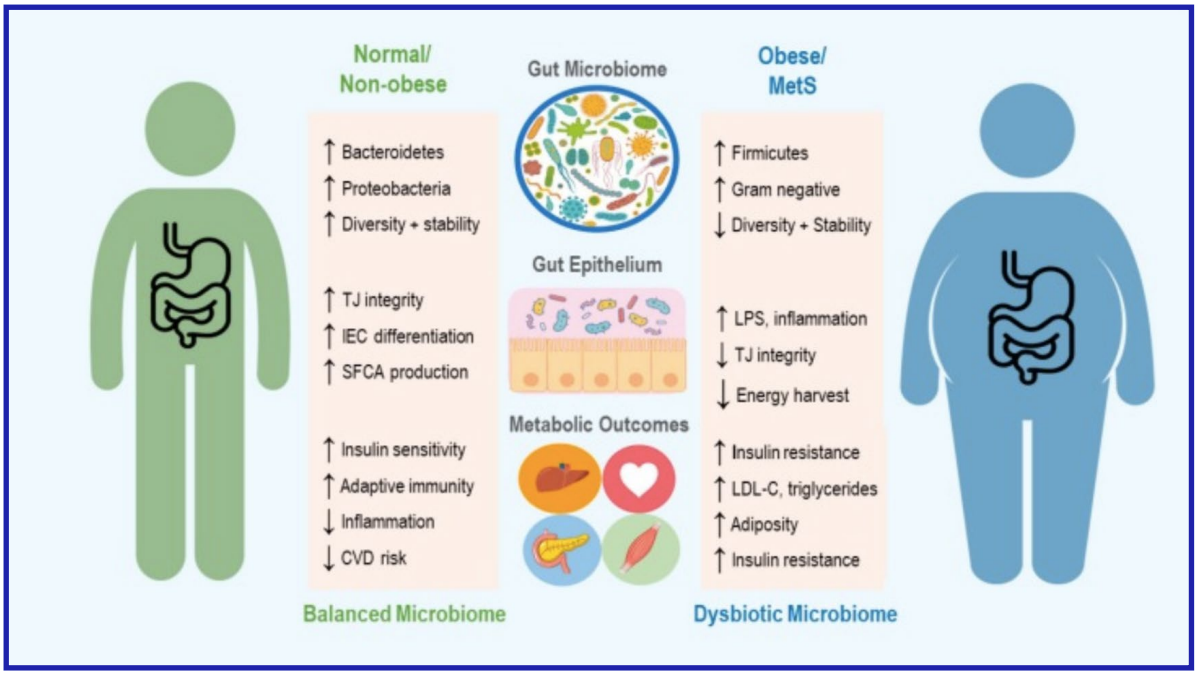
Additionally, short-chain fatty acids (SCFA), have far-reaching benefits, including:

- Improving long-standing dyslipidemia
- Providing fuel for intestinal epithelial cells (IEC)
- Modulating and regulating IEC proliferation and differentiation
- Impacting gut motility
- Strengthening the gut barrier
- Supporting immunomodulatory functions
- Facilitating gut endocrine host physiology[13]
- Playing a central role in the diet-gut microbiome-host metabolism axis[14]

Metabolic Syndrome and the Microbiome (continued)

It is clear that including the microbiome as part of a core strategy for working with MetS and its associated disorders is essential and may provide a sustainable solution for this global epidemic of obesity and rising rates of insulin resistance.

Microbiome health can be supported by modulating the microbiome with botanicals, diet, lifestyle changes, functional foods, and supplements.[15]



This figure from a 2020 review study by Green et al. summarizes the differences in microbiome-related metabolic effects in non-obese versus obese individuals.[16]

A study published in 2020 and conducted by Al Bander et al. concluded: "A vast pool of studies in animals and humans have indicated a critical interplay between the gut microbiota and inflammation that could inform therapeutic intervention for the treatment of these disorders."[17]

Clinical Pearl #1 – Include fiber

Research shows that high-fiber (plant-based) diets increase biodiversity and decrease non-favorable strains. On the other hand, high-fat diets seem to reduce protective SCFA production and increase concentrations of substances such as p-cresol, indole, arachidonic acid, and LPS in stools while increasing inflammatory markers in plasma. High-fiber diets, including fruits, vegetables, beans, nuts, and seeds, seemed to effect change in the microbiome in as little as five days. The Mediterranean diet has been closely associated with decreased rates of metabolic diseases and various cancers, mainly due to its fiber abundance.

Clinical Pearl #2 – Get your patients to move their bodies

While exercise provides beneficial physiological effects, movement also has a significant impact on microbiome health. Increased diversity in the microbiome and its antioxidant activity in the gut (due to increased levels of keystone probiotic species *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*) have a positive correlation with increased levels of aerobic and endurance exercise. Recommending a regular exercise routine along with dietary changes is imperative for influencing the microbiome and overall health.

Clinical Pearl #3 – Don't forget the mouth!

Research suggests that periodontitis may contribute to the development or exacerbation of metabolic syndrome. Patients with metabolic syndrome were 2.6 times more likely to develop periodontitis. Periodontitis leads to systemic inflammation, which can drive metabolic syndrome. Treating periodontitis has been shown to reduce circulating inflammatory mediators such as C-reactive protein and interleukin 6, and may serve as a beneficial therapeutic when addressing metabolic syndrome.

Clinical Pearl #4 – Include Detoxification Support

Detoxification is essential for maintaining optimal metabolic health, as it supports the body's ability to eliminate toxins that can interfere with cellular function, energy production, and hormone balance. When detoxification pathways are overwhelmed or impaired, toxic accumulation can contribute to insulin resistance, chronic inflammation, mitochondrial dysfunction, and metabolic disorders such as obesity and diabetes.

Most toxins are eliminated primarily through the liver via bile and the kidneys via the urine. Bile is released into the small intestines and these bile-bound toxins are destined for excretion in the stool. It is important to ensure healthy bile production and flow for optimal digestive function and toxin elimination.

Additionally, biofilms may harbor bacterial metabolites and toxins, including mycotoxins, and when biofilms are broken these toxins and metabolites may cause damage to the surrounding tissues or transient increases in inflammation. Including a binder, such as Biocidin Botanicals' G.I.Detox®+, can prevent the reabsorption of toxins and reduce the burden on the liver, making detoxification more efficient, improving the patient experience, and promoting compliance.

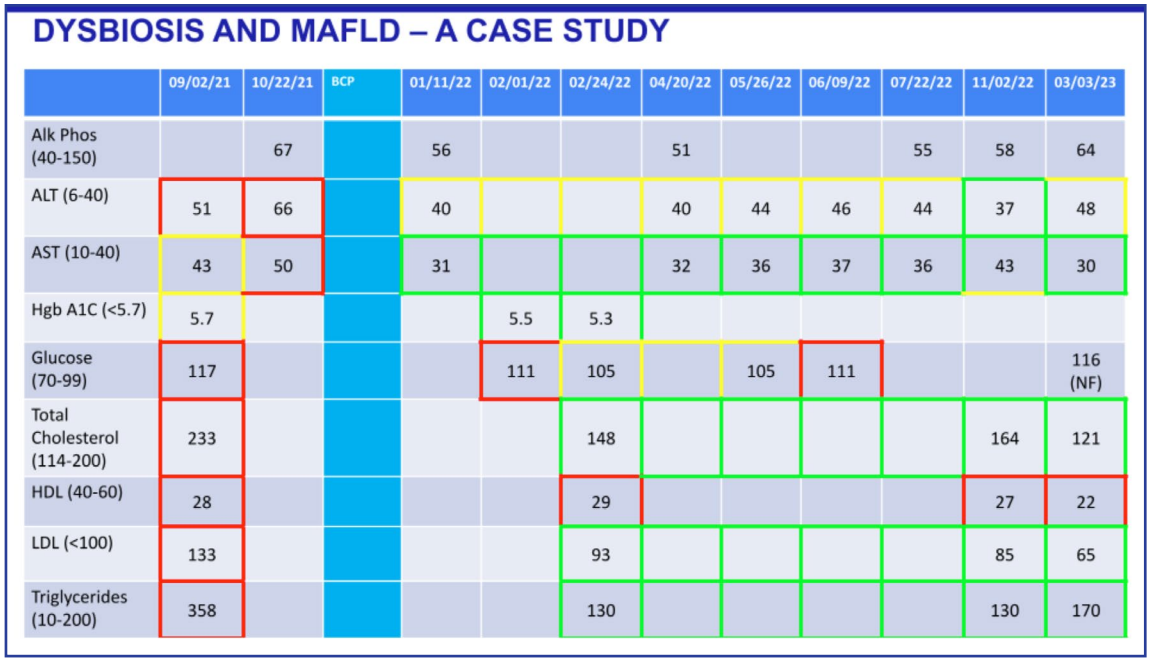
Optimize liver and kidney function

Additionally, consider including botanicals, such as those found in Liver GB+™, to support the liver and kidneys, including:

Artichoke	Stimulates bile flow, enhances fat digestion, supports detoxification, liver and kidney health
Milk Thistle	Enhances absorption, detoxification, and digestion, protects liver and kidneys
Turmeric	Helps support & stimulate bile flow, protects and supports the liver and kidneys
TUDCA	Supports healthy bile flow and gallbladder health, protects and supports the liver, thins bile, protects kidneys
Ginger	Improves production and flow of bile, promotes gastric emptying and reduces intestinal transit time, helps ease indigestion, belching, gas, and feelings of fullness after eating, and protects kidneys

MAFLD Case Study

The following case study outlines the journey of a 52-year-old male with a diagnosis of NAFLD. His protocol included the Bioclear® Microbiome Detoxification Program, and intermittent dietary changes progressing toward a lower carbohydrate/modified Paleo diet. Liver imaging was completed after one year on the program. The results illustrate the powerful role that microbial dysbiosis can play in the progression of metabolic issues.



Pre Bioclear® Program 3/15/21	Post Bioclear® Program 2/2/23
CAP (Steatosis) Score: 387 dB/m (**severe**)	CAP (Steatosis) Score: 293 dB/m (**mild**)
Fibrosis Score: 9.5 kPa (**significant**)	Fibrosis Score: 6.3 kPa (**insignificant**)

Lifestyle Recommendations

- Support your treatment with simple yet effective lifestyle recommendations. Check out the list contained in the Bioclear® Microbiome Detox Program Lifestyle Guide.
- Adopt a low inflammation diet (Modified Paleo, Mediterranean, etc.), that includes a high intake of non-starchy vegetables.
- Reduce overall caloric intake.
- Proactively work to lower stress.
- Increase exercise to support weight loss, blood sugar regulation, and cardiovascular health.

Therapeutic Plan Suggestions

Metabolic Syndrome/Insulin Resistance/Weight Loss Support		
CORE PROTOCOL		
Biocidin® Liquid or Capsules	Titrate to 15 drops 2x/day	Titrate to 2 capsules 2x/day
G.I. Detox®+	2 capsules at bedtime. 1 hour away from food, supplements, and medications. Temporarily increase dose to 2 capsules 2-3x/day if Herxheimer reaction observed/worsens.	
Proflora® 4R	1 capsule any time	
Liver GB+™	1 capsule 2x/day	
ADDITIONAL SUPPORT		
Olivirex®	Titrate to 2 capsules 2x/day	
Biotonic®	20 drops 2x/day	
G.I. InnerCalm®	1 stick pack mixed in water, 1-2 times daily, taken any time	
Dentalcidin®	2x/day	
Dentalcidin® LS	2 pumps 2x/day	
Dentalflora®	Dissolve 1 tablet in mouth daily at bedtime, at least 30 minutes away from other oral care, food, or drinks	

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

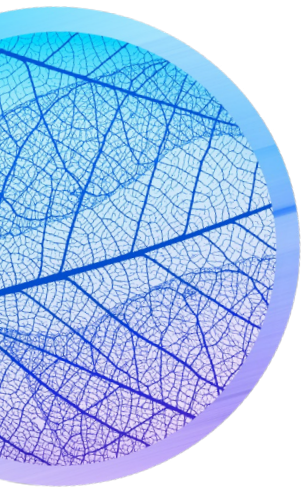
Additional Resources

RECOMMENDED BY DR. FILOMENA TRINDADE

Nutrient/Product	Key Actions*
Chromium	Reduces insulin resistance and helps reduce risk for CVD
Alpha-lipoic acid	Supports weight loss, improves insulin sensitivity, lowers blood pressure, and decreases atherogenic dyslipidemia
Curcumin	Anti-inflammatory, antioxidant, increases insulin sensitivity, decreases obesity, lowers leptin, and increases adiponectin
Berberine	Reduces blood glucose and blood lipids, increases insulin sensitivity, reduces inflammation
Omega-3 fatty acids	Lowers lipogenesis, increases fatty acid oxidation, regulates peroxisome proliferator-activated receptor-gamma
CoQ10	Antioxidant, mitochondrial support, reduces vascular oxidative stress
Vitamin D	Antioxidant activity, immunoregulatory
Magnesium	Enzymatic cofactor, vasodilatory, muscle relaxation, insulin metabolism, glucose control
Vanadium	Enhances insulin sensitivity, lowers blood sugar

Questions?

For clinical questions, email clinical@biocidin.com



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References

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Additional Resources

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