Diagnos-Techs Clinical & Research Laboratory Quarterly Newsletter

Spring
2015

ChronoBiology20

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Articles:

News:

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Diagnos-Techs wins Naturopathic Doctor News & Review 2015 Physician Choice Award for diagnostic laboratory excellence!

A Foundational Approach to Adrenal Restoration

Scott Buesing, ND

Restoring and optimizing adrenal function is often a priority for achieving patients' long-term wellness goals. It is common when testing adrenal function to find that a patient's adrenals are under or over-producing cortisol. Numerous options exist for improving adrenal function, including basic nutrients, herbal products, and direct hormone replacement. When trying to decipher these options, choosing the safest, most efficacious approach can be challenging.

In situations when cortisol levels are high, contributing factors should be identified. First, exposure to exogenous hormones needs to be ruled out. If an exposure is identified that occurred during testing, retesting is indicated to get true physiologic values. If cortisol appears to be high from endogenous production, further investigation is warranted. Elevations of cortisol, especially at night, can be diagnostic for Cushing's syndrome. Obtaining a relevant case history is necessary to rule in or rule out excess cortisol production from a tumor. Other testing may also be indicated. Once Cushing's syndrome, endocrine tumors, and exogenous exposures have been ruled out, many of the remaining cortisol elevations will be due to acute stressors, blood sugar problems, or underlying inflammation.

A careful case history and additional testing can usually uncover the culprits for elevated cortisol. Asking the patient what they experienced the day of testing can help identify situations where acute stressors were elevating values. In cases where cortisol is high due to acute stressors, phosphatidylserine and/or some of the treatments listed below for lowering cortisol can be considered.

Blood sugar problems are also commonly turned up on testing, the most typical pattern presenting with elevated first morning cortisol. It is hypothesized that individuals with blood sugar problems may not tolerate the drop in blood sugar levels that can occur overnight. If blood sugar levels fall during sleep, the adrenal glands will release cortisol to prevent blood sugar from falling too low. Many times this presents on testing with an elevated first morning cortisol. In situations where cortisol is elevated due to blood sugar dysregulation, stabilizing blood sugar is the primary strategy, rather than reducing cortisol directly.

In other cases, individuals suffering from pain and inflammation will also demonstrate elevated cortisol values on testing. If an individual describes having pain outright, or testing reveals elevated inflammatory markers, treating the cause of the inflammation may help normalize the cortisol response.

For the majority of patients, starting with nutrients and herbal formulations is appropriate for treating adrenal issues in general. Dosed properly, nutrients and herbs can restore function and help alleviate symptoms along with providing a wide margin of safety. Nutrients are the foundational support for the adrenals, helping to supply the constituents needed for the production of steroid hormones.

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20 &PROUD

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Nutrients critical for adrenal function include the following:

Pantothenic acid

Pantothenic acid has been shown in the research literature to raise cortisol levels.[1,2] It also appears to improve stress resiliency, acting as a modulating agent for adrenal function.[3] Pantothenic acid is a precursor for acetyl coenzyme A production, a compound essential for the production of corticosteroid hormones. In patients with low cortisol output, therapeutic dosing starts at 500mg twice daily. In patients for whom testing reveals both reduced and elevated cortisol values, pantothenic acid is not necessarily contraindicated, as it appears to improve the acute stress response.

Vitamin C

Higher doses (1 gram or more) of vitamin C appear to attenuate cortisol output in acute stressful situations.[4,5] Interestingly, the adrenals secrete vitamin C in response to stress along with cortisol.[6] Dosing is usually 500-1000mg or more for adrenal support.

Zinc

Zinc deficiency has been shown to impair a healthy stress response and zinc appears to moderate cortisol release.[7,8] In humans, stable zinc levels maintain stable cortisol levels postoperatively, preventing a sharp increase in cortisol.[9] Overall, zinc appears important in adrenal function. Safe long-term oral dosing is approximately 30mg daily, as doses from food and supplements exceeding 40mg can cause problems with copper deficiency.

Biotin

Research on biotin's effects on adrenal response are thin. One study in fruit flies demonstrated increased life span and improved stress resiliency.[10] Biotin is involved in regulation of genes involved in glucose metabolism, and clinical studies have shown improvement in blood sugar control with biotin supplementation.[11] There are a number of anecdotal case reports of biotin helping with energy levels and even fibromyalgia. Because of biotin's effects on regulating blood sugar, biotin is most indicated in cases with elevated first morning cortisol due to blood sugar problems, or other documented blood sugar or insulin dysregulation, although biotin is still worth considering in more general cases. Biotin is quite safe, and therapeutic dosing starts around 4mg (4000mcg) but can easily be increased to 8mg or more daily.

In addition to the above listed nutrients, consider a B-complex to help balance the formula.

Flavonoids

Flavonoids are a broad class of compounds found in numerous plants. Many flavonoid-rich plants have been shown to have beneficial effects on adaptation to stress and stress response including rooibos (*Aspalathus linearis*),[12] pomegranate (*Punica granatum*),[13] flax (*Linum usitatissimum*),[13] chocolate (*Theobroma cacao*)[14], and green tea (*Camellia sinensis*)[15], among others.

Combined with the basic nutrients, herbal adaptogens help to tailor the formula to an individual's needs. Some adaptogenic herbs to consider include:

Ginseng (*Panax ginseng*)

An herb with a long history of use, ginseng is typically considered a "hot" adaptogen, being more stimulatory than the other adaptogens for increasing energy levels. Due to its stimulatory effects, ginseng is worth considering in more fatigue-based cases that do not include anxiety symptoms. There is some concern that ginseng may raise blood pressure, although some studies have shown blood pressure lowering effects.[16]

Licorice (*Glycyrrhiza glabra*)

Licorice is the classic herb for adrenal support, with corticosteroid-sparing properties.[17] The main drawback with licorice is that it can deplete potassium by increasing mineralocorticoid activity, which can significantly raise blood pressure.[18] In individuals with hypertension it is contraindicated. When using licorice, blood pressure should be carefully monitored and recommendations could include increased potassium intake from food sources.

Siberian ginseng (*Eleutherococcus senticosus*)

Eleutherococcus, or siberian ginseng, is a more neutral herbal adrenal support. In sensitive individuals, it may be a better choice than some of the stronger or "hotter" herbal alternatives.

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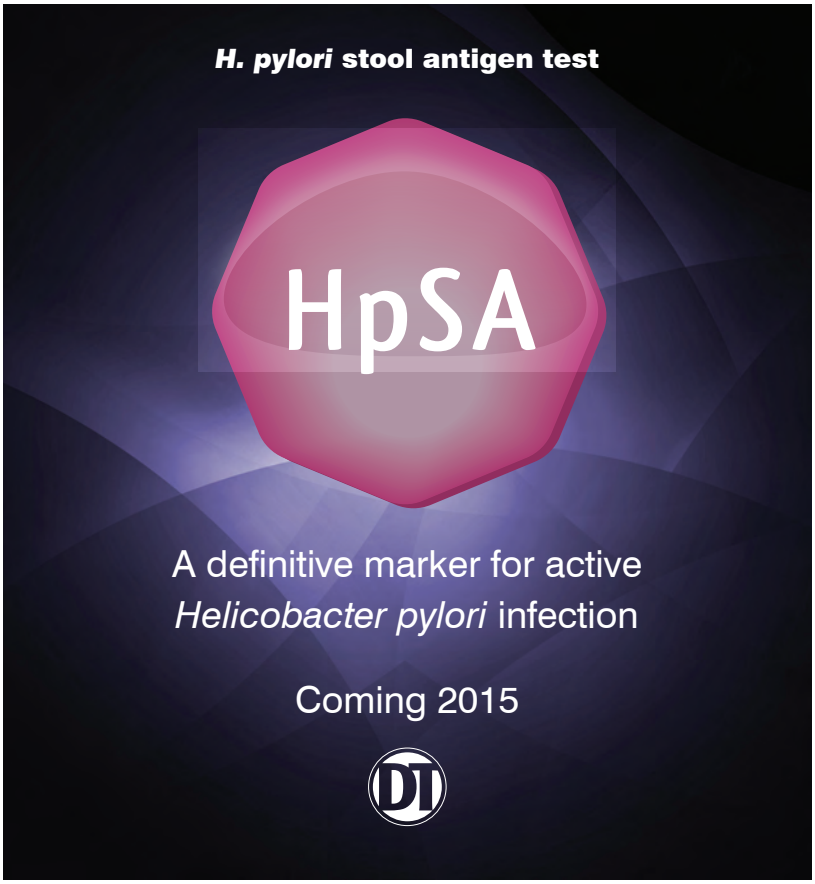


Tech Talk

Quarterly updates from our Diagnos-Techs Research & Development Team

Emerging evidence suggests that enterohemorrhagic ***E. coli*** **(EHEC)** strains can express one or both of two major forms of Shiga toxins (Stx1 and Stx2) and other virulence factors in various combinations that may have important clinical implications. Identification of these expression patterns is difficult to accomplish with traditional methods; however, polymerase chain reaction (PCR)-based assays can be used to screen clinical specimens for the presence of multiple specific DNA target sequences including the Shiga toxin gene variants. Look to Diagnos-Techs in the near future to add molecular diagnostics to the GI testing menu.

Dr. Dialogue *Current Medical topics*

DHEA

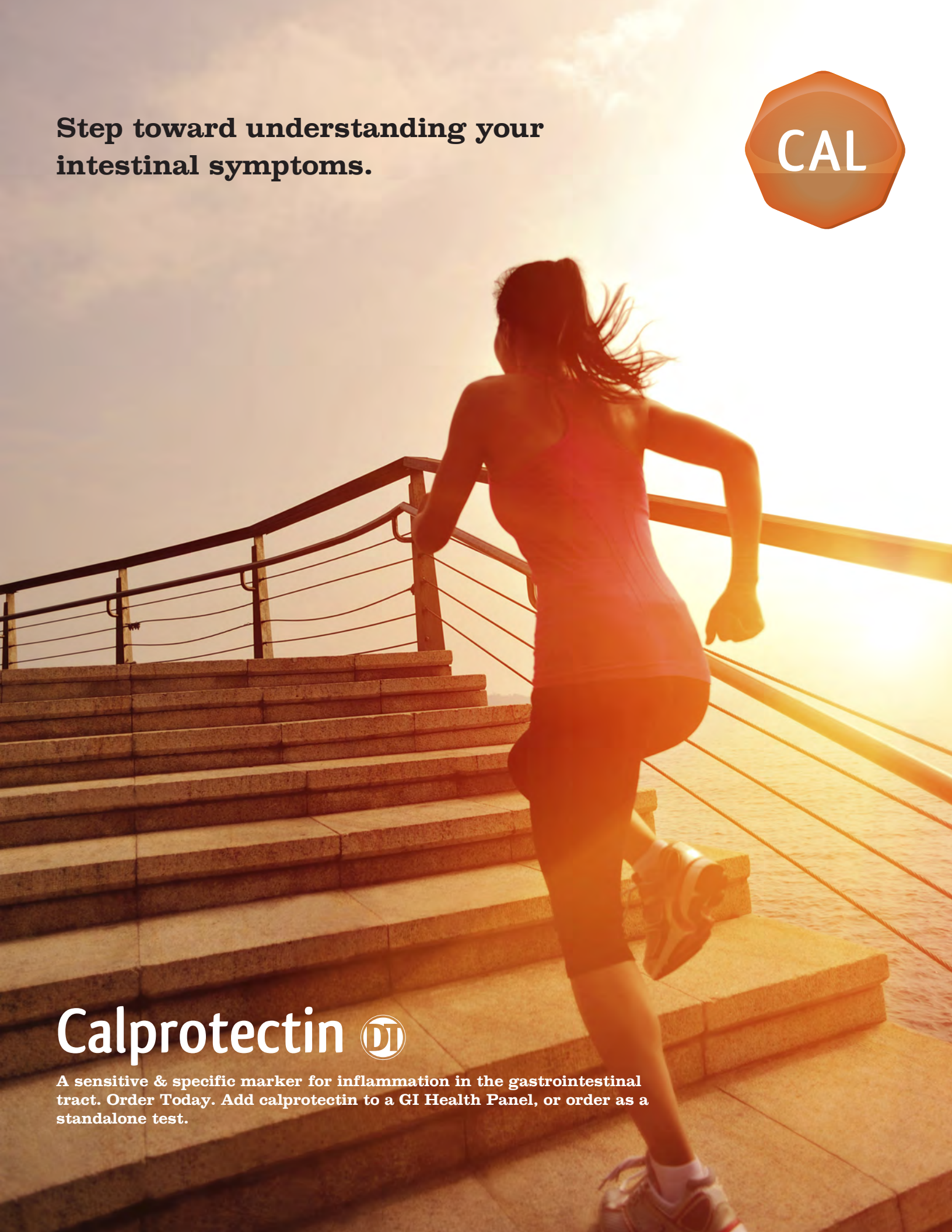
According to a recent study published in the *Journal of the American College of Cardiology*, low serum levels of DHEA and its sulfate (DHEA-S) may predict an increased risk of coronary heart disease in elderly men. This Swedish cohort study followed 2,416 men, aged 69-81 at baseline, over five years. After adjustment for potentially confounding risk factors (age, BMI, smoking, diabetes, hypertension, ApoB/A1 ratio, hs-CRP, eGFR), and adjustment for serum total testosterone and estradiol levels, the inverse association between serum DHEA/DHEA-S and risk of coronary heart disease remained significant.[1]

Bisphenol A

A new Korean study has found that exposure to bisphenol A (BPA) may raise blood pressure. This randomized, crossover study looked at the effects of BPA exposure from a canned soymilk beverage. Participants (n=60) were adult volunteers recruited from a local community center, aged ≥60, who ingested the same beverage in cans (high-BPA) or glass containers (low-BPA control) on separate study visits. Urinary BPA concentrations and systolic blood pressure were both significantly higher two hours after consumption of the canned beverage. Average systolic blood pressure increased by 4.5 mmHg after BPA exposure.[2]

Sedentarism

A recent analysis of data from the European Prospective Investigation into Cancer and Nutrition Study has found that overall inactivity (sedentarism) may be twice as deadly as obesity (high BMI). This multicenter prospective cohort study analyzed data from 334,161 men and women, aged 25-70 at baseline, who were followed over 12 years. Height, weight, BMI, and waist circumference (WC) were tracked, along with self-reported activity levels. Researchers found that physical activity was inversely associated with all-cause mortality at all levels of BMI and WC. The greatest reduction in risk was observed in the comparison of inactive and moderately active groups. Risk of early death was reduced 16 to 30% in people who were at least moderately active, regardless of weight, BMI, and WC. Researchers conclude that overall physical inactivity may be responsible for as many deaths as abdominal adiposity (elevated WC), and for twice as many total deaths as high BMI.[3]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Ashwagandha (*Withania somnifera*)

Another herb with a long history of use in Ayurvedic medicine, ashwagandha is one of the more relaxing adrenal restoratives.[19] In individuals with lower adrenal output and anxiety or depression, ashwagandha can be helpful. Ashwagandha has been shown in animal studies to raise active thyroid hormone levels,[20] and there is one case report of thyroid toxicosis associated with its use.[21] Overall, the herb appears quite safe; however, in autoimmune thyroid cases caution should be applied.

Rhodiola (*Rhodiola rosea*)

Rhodiola is an adaptogen that has research supporting its use for mental emotional symptoms. Preliminary studies appear to indicate that beyond acting as an adaptogen, rhodiola may help with depression and anxiety.[22, 23] In individuals struggling with lowered adrenal output and mental emotional symptoms, rhodiola may help improve functioning on multiple levels.

Maca (*Lepidium meyenii*)

Research into maca is just starting to demonstrate its potential for helping with hormonal issues in women.[24] In cases that include perimenopausal or postmenopausal symptoms, maca may be a good choice for helping both with restoring adrenal function and decreasing hormonally-related symptoms.

Adrenal glandulars, pregnenolone, DHEA, and cortisol replacement

Other options for treating lowered adrenal function exist, including adrenal glandulars, pregnenolone, DHEA, and direct cortisol replacement. The main concern with these treatments is based on the potential for suppression of endogenous hormone production. Adrenal glandulars (desiccated adrenal) may contain adrenal hormones including cortisol, epinephrine, and norepinephrine, just as desiccated thyroid contains active thyroid hormones. The risks from pregnenolone and DHEA are probably low when used in more conservative doses, but suppression has not been well researched. When cortisol is administered, it provides negative feedback on the hypothalamic axis, decreasing endogenous production. In some cases, this down-regulation may be long-standing or permanent. The amount of cortisol in any glandular product is not listed on the label, since the FDA does not allow supplements with known amounts of cortisol to be sold over-the counter. Therefore, amounts of cortisol in glandular products are usually unknown and the risk of adrenal suppression, while likely low, is difficult to estimate.

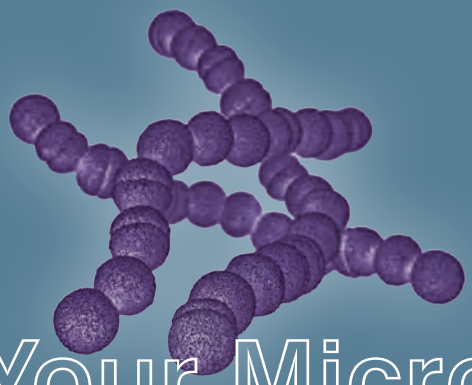
In cases where adrenal function does not improve with standard treatment and lifestyle adjustments, and symptoms are severe enough to negatively influence quality of life, pregnenolone, DHEA, or cortisol replacement can be considered. Pregnenolone is most indicated with low cortisol combined with low 17-OH progesterone, which is a precursor to cortisol. Pregnenolone usually works to raise cortisol, although it can raise other hormone levels as well. If used for more than a couple months, checking all the downstream hormones for dysregulation is warranted. Dosing of pregnenolone to raise cortisol is usually up to 1mg/kg per day. For DHEA, treatment is most indicated with low measured DHEA levels. DHEA is not a precursor to cortisol; it increases DHEA and other downstream hormones. Dysregulation of downstream hormones with DHEA use is common in both men and women, and hormone levels should be monitored. Dosing is usually increased slowly, starting at 5mg and increasing in 5mg increments, with a maximum dose of 10mg for women and 25mg for men.

If cortisol is utilized, patients should be made completely aware of the risk/benefit ratio through proper informed consent. One study appeared to indicate that dosing of 5 to 10mg of hydrocortisone daily for one month did not lead to significant adrenal suppression.[25] Another study utilizing dosing of 13mg/m^2 (approximately 20-25mg daily based on body surface area) of hydrocortisone for 12 weeks documented suppression of cortisol production in close to half of treated patients.[26] Combining cortisol with nutrients and herbs with the goal of using cortisol for the shortest duration would likely provide greater safety than stand-alone long-term cortisol supplementation.

Typically, an effective treatment approach should show clinical and laboratory results by three months. Always take into account if an individual has life stressors that are not well managed and consider other lifestyle factors including exercise, diet, and social interactions. Symptom improvement is not necessarily quick, taking place over weeks to months, making it important to set patients' expectations appropriately.

Restoring adrenal function in patients can provide a number of benefits. Knowing the options available can enhance effective treatment strategies for managing patients' symptoms and improving their well-being.

*Medical references can be found at diagnostechs.com/Pages/NewsLetter.aspx



Meet Your Microbiota

Quarterly updates from our Diagnos-Techs Microbiology Team

As our knowledge of the human intestinal microbiota expands, our understanding of the roles and pathogenicity of various organisms continues to grow and change. Using advanced MALDI-TOF technology to identify bacteria in stool, we gain access to valuable information about gut flora, including the ability to identify over 2,000 different organisms. While some generalizations can be made about various bacteria, there are often exceptions, and in many cases an organism may be considered commensal as well as opportunistic. In this new section of our newsletter, we examine the current research on organisms that you may find reported on your patients' Bacterial Stool Culture results.

The human intestinal tract contains up to 100 trillion microbial cells, most of which are found in the large intestine. These microorganisms are crucial for proper digestive function. Gut microorganisms break down undigested carbohydrates into short chain fatty acids, which are readily absorbed in the colon. The most important of these fatty acids are butyrates utilized by colonic cells, acetates used by the muscle tissues, and propionates that are used by the liver. Intestinal microorganisms also play a role in synthesizing vitamins such as vitamins B and K, as well as metabolizing bile acids, sterols, and other compounds.

Resident microflora also help protect the human host from disease by outcompeting small numbers of more virulent organisms. Without the resident commensal microflora, the GI tract would be much more prone to disease.

When we receive a stool sample here in the laboratory, we perform tests to rule out the presence of known enteric bacterial pathogens that may cause acute or chronic disease. We also plate the stool sample on several types of aerobic culture media in order to make an assessment of the bacterial flora present in the patient's intestinal tract.

From these aerobic culture plates, we report and quantify the mixed gram positive and mixed gram negative flora. These gram positive and gram negative flora include the various normal resident intestinal bacterial species. We expect to find moderate to heavy growth of both gram negative and gram positive bacteria from normal stool samples.

The Diagnos-Techs' Bacterial Stool Culture report lists the most prevalent organisms within the mixed flora. Up to three individual organisms will be listed and quantified. This allows the clinician to check for the prevalence of certain commensal and beneficial microorganisms and for any opportunistic pathogens, as well as to compare the composition of the mixed flora to previous cultures sent to Diagnos-Techs.

The most commonly reported organisms are nontoxigenic *E. coli* and *Enterococcus* species. Nontoxigenic *E. coli* is the resident *E. coli* that tests negative for production of Shiga toxins. Nontoxigenic *E. coli* is the most prevalent gram negative aerobic organism found in the stool of healthy individuals.

Gram positive bacteria commonly reported include various *Enterococcus* and *Streptococcus* species. These gram positive organisms are sometimes found in stool samples from healthy individuals and may be considered commensal; however, certain species (and strains) may be considered opportunistic when associated with GI symptoms and illness.

Please watch for updates on opportunistic bacteria and enteric pathogens in our upcoming issues of ChronoBiology.

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Upcoming Events:

NWNPC 2015
- 59th Annual Convention
- May 1-3, 2015 • Seattle, WA

Bastyr University
- Product Showcase
- May 13, 2015 • Kenmore, WA

AANP
- 30th Annual Conference
- Aug 5-8, 2015 • Oakland, CA

Monthly Webinar Schedule:

April 16th, 2015
Healthy Aging Series: Cancer Prevention Part 3
Dr Lisa Canar

May 14th, 2015
Eating Disorders: An overview, including noninvasive testing
Dr Scott Buesing

June 11th, 2015
Insulin Resistance and Blood Sugar Dysregulation: A clinical update
Dr Scott Buesing

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**Medical references can be found at diagnostechs.com/Pages/NewsLetter.aspx*

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Doctor Dialogue #20

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