The concept of stress has invaded our social and biological reality of being human. Most often, we equate "stress" with stressful events (loss of family member, divorce, major life changes). Yet, from a physiological perspective, the definition of stress and its effects are much more difficult to grasp. What is clear is that stress takes a toll on the body in ways we are only beginning to understand. In fact, some researchers claim nearly 75 to 90% of the diseases prevalent in Western society today are somehow related to the stress mechanisms of the body.

For many patients, stress is a major underlying cause of several mental and physical health problems (Figure 1). It is the daunting task of the clinician to determine which patients are becoming overwhelmed by the effects of stress as well as develop individualized support protocols to help patients regain their wellbeing. The ARK Stress Recovery Program is designed to help you and your patients easily identify, assess and manage the effects of stress and dysfunction within the body's stress-response system.

The clinical case studies included in this in-practice guide are intended to provide clinicians with guidelines for natural solutions to help reverse the negative effects of stress. This includes protocols for each of the three stages of HPA axis dysfunction, as well as protocols and lifestyle recommendations addressing each of the four key stressors that exacerbate HPA axis dysfunction (Figure 2).

---

**Figure 1: Ten Patient Symptoms Indicating Possible HPA Axis Dysfunction**

1. **Fatigue**  
   - The most common presenting complaint

2. **Pain**  
   - Chronic pain in the joints  
   - Headaches  
   - No response to pain therapies

3. **Mood regulation**  
   - Depressed mood  
   - Anxious thoughts  
   - Restless mind

4. **Female hormone disorders**  
   - PMS  
   - Infertility  
   - Perimenopause  
   - PCOS

5. **Insomnia**  
   - Difficulty getting to sleep  
   - Trouble staying asleep

6. **Allergies**  
   - Runaway immune dysfunction without adequate cortisol

7. **Asthma**  
   - Chronic inflammatory condition

8. **Thyroid disorders**  
   - Often mimic HPA axis dysfunction

9. **Hypoglycemia**  
   - Lightheadedness  
   - Brain fog  
   - Headaches  
   - Sleepiness

10. **GI disturbances**  
    - Constipation  
    - Diarrhea  
    - Heartburn  
    - Reflux  
    - Bloating/Gas

---
Introduction

Each clinical case study in this in-practice guide includes sample test results, plus principles and treatment protocols for consideration when initiating salivary hormone assessments and therapeutic lifestyle applications for the treatment of HPA axis-related dysfunction in chronically ill patients.

Additionally, the ARK In Practice section (page 22) offers guidelines for utilizing the resources provided in the ARK Clinical Implementation Resource Kit. These easy-to-use tools will help you create a streamlined and comprehensive stress recovery program in your practice. Please refer to Appendix D, The ARK In-Practice Revenue Generation Model (page 70), for a basic outline of annual revenue generation using the ARK Stress Recovery Program in your practice.

Additional Educational Resources

The ARK Stress Recovery Program In-Practice Guide provides an overview of HPA axis dysfunction and clinical case studies and protocols. The Role of Stress and the HPA Axis in Chronic Disease Management, written by Thomas G. Guilliams, Ph.D., provides a comprehensive review of HPA axis dysfunction and the latest research on this topic. As such, it serves as an excellent companion to the ARK In-Practice Guide, and referrals to specific research or chapters are included throughout. To purchase The Role of Stress and the HPA Axis in Chronic Disease Management, please visit LifestyleMatrix.com/ARKProgram.

Summary of Objectives for the ARK In-Practice Guide:
- Identify a three-stage diagnostic paradigm through correlations of testing and symptom questionnaires
- Provide sample interpretations of common salivary cortisol and DHEA tests
- Offer suggested protocols for each stage of HPA axis dysfunction and each of the key stressors
- Offer suggested protocols for patients with HPA axis dysfunction and hypothyroidism
- Offer suggested protocols for using HPA axis support with bio-identical hormone replacement therapy
While it may seem obvious to most, biologists have not agreed on the definition of “stress” for more than 75 years. Does stress define the necessary adaptations to stressors, or the dysfunctions associated with failing to adapt to those stressors? How much stress is “normal” or even necessary to maintain the stress-response system? When we think of stress, we most often think of negative stress, or as some would say, “distress;” but positive events (wonderful surprises, passion, athletic competition) can elicit seemingly identical responses from a physiological perspective.

The preeminent scientist who brought the concept of stress to the forefront of medical discussion was Hans Selye. His book, The Stress of Life, written for the lay audience, popularized the notion of stress as the general response to a wide variety of insults. His research, mostly with rats, revealed a recurring set of physiological outcomes (i.e., hypertrophy of the adrenal gland, atrophy of the lymphatic organs and ulcers in the stomach) in response to stress. He later formed what he called General Adaptation Syndrome (GAS) in a three-stage format:

**General Adaptation Syndrome (GAS)**

1. **The alarm reaction**, which involves increased adrenocortical secretion and activation of the sympathoadrenal system.
2. **The stage of resistance**, which involves the balancing of the adrenocortical hormones’ effect on water and electrolyte balance and carbohydrate metabolism. It is the “true adaption” to stress.
3. **The stage of exhaustion**, which involves the depletion or exhaustion of the adrenal glands’ ability to make corticosteroids.

We recognize that Selye has simplified a complex set of responses and that the GAS has some limitations in defining the progression of all stress-related HPA axis abnormalities. However, this three-stage model is still the basis of much of the HPA axis stress-related research to this day. A similar three-stage model is incorporated into the ARK Stress Recovery Program paradigm.
The modern study of stress has identified three stages of hypothalamic-pituitary-adrenal (HPA) axis dysfunction, also known as the General Adaptation Syndrome.
How to Successfully Implement the ARK Stress Recovery Program in Your Practice

First Appointment:
1. During the first appointment, the patient completes the 4 Key Stressors Questionnaire (page 26).
2. While the patient is waiting to see you, the patient watches the ARK Whiteboard Education video as an introduction into how stress impacts health.
3. A. Using the presentation pads, discuss the basic physiology of the HPA axis and the importance of testing to identify the patient's stage of HPA axis dysfunction. Also, review the symptoms and overall cortisol/DHEA patterns typically observed in each stage.
   B. Review the 4 Key Stressors Questionnaire and determine the key stressors driving HPA axis dysfunction.
   C. Begin the patient on the initial treatment protocol, including the comprehensive formulation to address key stressor(s).
4. Patient receives the ARK Stress Recovery Program Patient Handbook. Instruct the patient to read the first ten pages of the handbook, along with the chapter correlating to their key stressor(s). The patient should implement the applicable lifestyle and nutritional recommendations and bring questions to the next appointment.
5. The patient goes home with a test kit to assess HPA axis dysfunction (cortisol, DHEA imbalances) as well as additional hormone testing (estrogen, progesterone, testosterone and/or thyroid hormone imbalances) if necessary.

Follow-Up Visit (2-3 Weeks)
6. A. Review steps patient has taken to improve nutrition and implement lifestyle change along with any questions the patient has on integrating these steps based on information read in the patient handbook.
   B. Review test results along with patient history to identify the patient's specific stage of HPA axis dysfunction.
   C. Patient receives a treatment strategy based on their symptoms, stage of dysfunction and specific cortisol/DHEA imbalances. Patient continues the product chosen during the first office visit to address their underlying key stressor.
   D. Although the nutritional supplementation protocol will likely improve patient symptomology, it is important to set patient expectations by reinforcing that if no lifestyle change is implemented, improvement in HPA axis dysfunction will be inhibited.

Follow-Up Visit
7. Within three months of implementing the initial protocol, the patient should be offered a salivary hormone re-test, provided there has been significant symptom change, as well as lifestyle change. Reinforcing the proper changes, as mentioned in Step 6, is crucial to improvement upon retesting. Consider waiting to retest until these steps have been properly implemented by the patient.
ARK In-Practice Revenue Generation

The ARK Stress Recovery program can be a source of significant revenue generation for any clinical practice or integrative pharmacy. Now that you have reviewed how to use the tools and resources provided in your ARK Clinical Implementation Resource Kit, please refer to Appendix C (page 68) to review an outline of an annual revenue generation model integrating office visits, testing, product sales, and Group Visits. This model can be adjusted per your individual practice model.

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**Initial In-Office Visit**

**STEP 1** Patient completes the 4 Key Stressors Questionnaire

**STEP 2** Patient watches the ARK Whiteboard Patient Education Video

**STEP 3**

A. Clinician utilizes presentation pads to discuss the physiology of the HPA axis and the importance of identifying the patient’s stage of dysfunction

B. Clinician and patient identify key stressor(s):

C. Patient begins comprehensive formula to address key stressor(s)

**STEP 4** Patient receives ARK Patient Handbook

It is recommended that patients review the first 10 pages of the handbook and the chapter correlating with their key stressor(s).

- **Chapter 1**: Blood Sugar Control
- **Chapter 2**: Mental & Emotional Stress
- **Chapter 3**: Overcoming Insomnia
- **Chapter 4**: Reducing Inflammation

The patient should also review the lifestyle and nutritional recommendations outlined in each chapter.

**STEP 5**

A. Patient goes home with lab test kit to assess HPA axis function

B. Clinician encourages long-term lifestyle changes to begin immediately
A. Clinician reviews test results, questionnaire and patient history in order to identify stage of HPA axis dysfunction.

B. Clinician develops treatment strategy based on patient’s stage of HPA axis dysfunction.

### Stage 1: Hyper-Cortisol
- DHEA is borderline low, low or normal
- Total cortisol sum is high
- At least one cortisol is high

### Stage 2: Cortisol-Dominant
- DHEA is borderline low or low
- Total cortisol sum is normal
- Morning, noon or afternoon cortisols are borderline low or low

### Stage 3: Hypo-Cortisol
- DHEA is borderline low or low
- Total cortisol sum is low
- Most cortisols are borderline low or low

At this time, consider enrolling patients in a Group Visit. We recommend Restoring the Balance: Stress Hormones and Health. See the following page for more details.
In 3-4 months, the clinician retests the patient to track progress, and adjusts the treatment strategy as needed.

Follow-Up Visit (3–4 Months)

**ADRENAL STRESS PROFILE**

- **DAY 1**
- **DAY 90**

TRANSFORMING MEDICINE WITH GROUP VISITS

During the two to three months that patients are implementing appropriate lifestyle recommendations and waiting to retest, it is highly encouraged to host Group Visits, especially at months one and two. Group Visits will help keep patients engaged and encouraged prior to the one-on-one visits to reassess their progress. This is a great time to reinforce healthy lifestyle patterns and motivate patients. We recommend using *Restoring the Balance: Stress Hormones and Health*. You can find this and other GVTs at TheLifestyleMatrix.com.
The hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-thyroid (HPT) axis are closely connected (Figure 6). Imbalances in one system often cause an imbalance in the other. Symptom overlap is also common including fatigue, chronic pain, weight gain, depression and memory problems, and menstrual irregularities. When looking at a patient’s list of symptoms, it is difficult to determine without testing whether the HPA and/or HPT axis are affected. Due to the overlap of both of systems, it is important to look at the HPA axis in every case we suspect thyroid issues.

Primary thyroid dysfunction occurs when the tissues are not able to produce hormone levels adequate for hypothalamic/pituitary demands, which may be brought on by Hashimoto’s thyroiditis, an autoimmune condition, or nutritional deficiencies such as lack of iodine, or iatrogenic causes. More commonly, secondary thyroid suppression is due to reduced signaling from the hypothalamus and pituitary. This is characterized by normal to low (TSH) levels, even when the patient has low or low normal T4 and T3. This secondary thyroid suppression is a direct result of the hyperactivation of the HPA axis and the production of cortisol and should be interpreted as a self-defense mechanism against rapid breakdown. When this situation exists, as it often does, a prudent clinician should exercise caution before increasing exogenous hormone doses simply because the patient has requested to do so. Prolonged overuse of thyroid hormone therapy risks premature breakdown of tissues, particularly in bone mineral density.

**Figure 6: Stress and the HPT Axis**

1. As stress activates the HPA axis, corticotropin-releasing hormone (CRH) is released from the hypothalamus in the brain. CRH release directly inhibits the release of thyroid-stimulating hormone (TSH), resulting in a decrease in thyroid hormone output.

2. Chronic stress generates excess release of cortisol. This induces a catabolic state and inhibits the release of TSH.

3. Cortisol inhibits conversion of T4 to T3 and promotes conversion of T4 to reverse T3 (RT3). RT3 decreases T3 activity by competitively antagonizing T3 at the receptor level.
Clinical Case Studies Associated with the Three Stages of HPA Axis Dysfunction

Stage 1: Hyper-Cortisol

Sample Test Result 1-1

Patient Symptoms
The patient is experiencing anxiety during the day, restlessness in the evening, works an excessive number of hours, often feels wired and is a “Type A” personality.

First Office Visit
Patient starts with a neurotransmitter support formula to help increase serotonin, GABA, and alpha brain wave activity to help combat feelings of anxiety and restlessness and help reduce HPA axis activation caused by mental stress. Patient receives a copy of the ARK Stress Recovery Program Patient Handbook and is instructed to read Chapter 2: Mental and Emotional Stress and review the lifestyle recommendations for relieving stress.

Test Results

<table>
<thead>
<tr>
<th>Cortisol Readings:</th>
<th>Units</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning (6:00 – 8:00 a.m.)</td>
<td>30.0  nM</td>
<td>13.0 – 24.0 nM</td>
</tr>
<tr>
<td>Noon (12:00 – 1:00 p.m.)</td>
<td>14.6  nM</td>
<td>5.0 – 8.0 nM</td>
</tr>
<tr>
<td>Afternoon (4:00 – 5:00 p.m.)</td>
<td>15.4  nM</td>
<td>4.0 – 7.0 nM</td>
</tr>
<tr>
<td>Nighttime (10:00 p.m. – 12:00 a.m.)</td>
<td>9.2   nM</td>
<td>1.0 – 3.0 nM</td>
</tr>
<tr>
<td>Cortisol Sum (10:00 p.m. – 12:00 a.m.)</td>
<td>69.2  nM</td>
<td>23.0 – 42.0 nM</td>
</tr>
<tr>
<td>DHEA-S Average (10:00 p.m. – 12:00 a.m.)</td>
<td>3.0   NG/ML</td>
<td>2.0 – 10.0 NG/ML</td>
</tr>
</tbody>
</table>

HPA Stress Profile

Stress Profile

- Stressed and wired
- Severe anxiety
- Total cortisol sum is high
- DHEA is on low end of normal
Clinical Case Studies Associated with the Three Stages of HPA Axis Dysfunction

Primary Protocol: Hyper-Cortisol

First Office Visit

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage Range</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HTP</td>
<td>75-300 mg/day</td>
<td>• Directly converts into serotonin in the brain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increases serotonin production, promotes a positive mood and decreases anxiety</td>
</tr>
<tr>
<td>PharmaGABA*</td>
<td>100-400 mg/day</td>
<td>• Natural form of GABA, found to promote a relaxed state by increasing alpha waves and decreasing beta waves in the brain</td>
</tr>
<tr>
<td>L-theanine</td>
<td>100-400 mg/day</td>
<td>• Amino acid naturally found in green tea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increases serotonin and dopamine activity in the brain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Promotes relaxation by increasing alpha brain wave activity</td>
</tr>
<tr>
<td>L-taurine</td>
<td>100-1,000 mg/day</td>
<td>• Amino acid that calms the nervous system by binding to GABA receptors and activating glycine receptors in the brain</td>
</tr>
<tr>
<td>Magnesium</td>
<td>100-600 mg/day</td>
<td>• Required to produce serotonin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Promotes relaxation by blocking excitatory glutamate (NMDA receptors)</td>
</tr>
</tbody>
</table>

Second Office Visit (following a review of test results)

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage Range</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHEA</td>
<td>5 mg (1-3 times per/day)</td>
<td>• Improves mood regulation and provides antagonist activity against elevated glucocorticoids</td>
</tr>
<tr>
<td>Phosphatidyserine</td>
<td>100-600 mg</td>
<td>• Reduces elevated cortisol levels by blunting ACTH release within the HPA axis</td>
</tr>
<tr>
<td>Ashwagandha</td>
<td></td>
<td>• Adaptogenic herb that helps to balance cortisol levels and reduce perceived stress and anxiety</td>
</tr>
<tr>
<td>Eleuthero</td>
<td></td>
<td>• Adaptogenic herb used to help improve mental and physical fatigue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Shown to help improve mental performance during stress</td>
</tr>
<tr>
<td>Rhodiola</td>
<td></td>
<td>• Adaptogenic herb found to support mood, memory and mental performance while decreasing anxiety</td>
</tr>
</tbody>
</table>

Protocol Summary
This sample test report is reflective of high mental and emotional stress levels causing hyper-excretion of cortisol within the HPA axis. The suggested protocol utilizes the combination of adaptogenic botanicals and phosphatidyserine to help improve resistance to stress and lower excess cortisol levels. The inhibitory neurotransmitter support therapy using amino acids that increase serotonin and GABA activity will help improve stress perception and reduce anxiety and restlessness. DHEA supplementation is crucial, as the cortisol sum relative to DHEA level is very high. The glucocorticoid antagonist mechanisms of DHEA protect against the neurological effects of excess cortisol in the brain as well as tissue breakdown. Additional phosphatidyserine can be used in the evening, particularly if the patient is reporting frequent waking throughout the night. From a lifestyle standpoint, reinforcing the stress reduction techniques outlined in Chapter 2 of the ARK Stress Recovery Program Patient Handbook and prescribing specific strategies, such as scheduling downtime or taking part in relaxing exercises, will further improve symptoms and speed up HPA axis recovery.
Sample ARK In-Practice Revenue Generation Model

The following tables provide a general model for revenue generation based on each patient that is run through the ARK Stress Recovery Program for six months. This includes a first and second office visit, baseline and follow-up salivary hormone tests, a group visit, as well as a six months’ supply of supplements for HPA axis support.

The revenue generation models below include an insurance-based model (Table A) and a cash practice model (Table B). The five indications for administering a test kit include fatigue, insomnia, anxiety, depression, hypothyroidism, and menopause/HRT, a Group Visit, as well as the 10 Patient Symptoms Indicating Possible HPA Axis Dysfunction (Figure 1, page 2).

Table A: Revenue Generation Based on Insurance Model

<table>
<thead>
<tr>
<th>Service</th>
<th>Fee</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>First office visit</td>
<td>$150</td>
<td>$220 bill sent to insurance for new patient E&amp;M code #99203 or established patient code #99214 billed on time, with roughly 70% gross collection</td>
</tr>
<tr>
<td>Approximate initial supplement sales profit</td>
<td>$112</td>
<td>Products may include, but not limited to: adaptogenic blends, neurotransmitter support formulas, phosphatidylserine, DHEA</td>
</tr>
<tr>
<td>Salivary hormone test kit (initial baseline test)</td>
<td>$100</td>
<td>Paid at the front desk—part administrative/part evaluation fee, not billed to insurance</td>
</tr>
<tr>
<td>Second office visit</td>
<td>$150</td>
<td>$220 bill sent to insurance for E&amp;M code #99214 billed on time with roughly 70% gross collection</td>
</tr>
<tr>
<td>Group Visit</td>
<td>$60</td>
<td>Bill a level 3, 99213 CPT code. Billing is based on complexity, not time in a Group Visit. See Figure 8 for additional information regarding Group Visits</td>
</tr>
<tr>
<td>Supplement sales profit for 5-month refills</td>
<td>$560</td>
<td></td>
</tr>
<tr>
<td>Salivary hormone kit #2 (Re-test in 3-4 months)</td>
<td>$100</td>
<td>Paid at the front desk—part administrative/part evaluation fee, not billed to insurance</td>
</tr>
<tr>
<td><strong>Total profit from 6-month ARK Program (per patient)</strong></td>
<td><strong>$ 1,232</strong></td>
<td></td>
</tr>
</tbody>
</table>

Based on the insurance model, if, each week, the practice has one patient starting and adhering to a six-month ARK Stress Recovery Program, the total revenue generated will be $64,064 in 12 months.
Table B: Revenue Generation Based on Cash Practice Model

<table>
<thead>
<tr>
<th>First office visit</th>
<th>$220</th>
<th>Based on 30-minute office visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approximate initial supplement sales profit</td>
<td>$112</td>
<td>Products may include, but not limited to: adaptogenic blends, neurotransmitter support formulas, phosphatidylserine, DHEA</td>
</tr>
<tr>
<td>Salivary hormone test kit <em>(initial baseline test)</em></td>
<td>$100</td>
<td>Based on a $100 mark-up for each test kit (paid by patient)</td>
</tr>
<tr>
<td>Supplement sales profit for 5-month refills</td>
<td>$560</td>
<td></td>
</tr>
<tr>
<td>Second office visit</td>
<td>$220</td>
<td>Based on 30-minute office visit</td>
</tr>
<tr>
<td>Group Visit</td>
<td>$75</td>
<td>See Figure 8 for additional information regarding group visits</td>
</tr>
<tr>
<td>Salivary hormone kit #2 <em>(re-test in 3-4 months)</em></td>
<td>$100</td>
<td>Based on a $100 mark-up for each test kit (paid by patient)</td>
</tr>
<tr>
<td><strong>Total profit from 6-month ARK Program (per patient)</strong></td>
<td><strong>$1,387</strong></td>
<td></td>
</tr>
</tbody>
</table>

Based on the cash practice model, if, each week, the practice has one patient starting and adhering to a six-month ARK Stress Recovery Program, the total revenue generated will be $72,124 in 12 months.

### Restoring the Balance: Stress Hormones and Health Group Visit Toolkit

Following the second office visit, it is recommended to have the patient set up their next appointment with you approximately one month later in a Group Visit. Group Visits help to maximize your time with patients who need lifestyle education. The **Restoring the Balance: Stress Hormones and Health Group Visit Toolkit** provides the necessary components to implement and conduct a successful Group Visit Model in your practice. The tools include the SOAP note, patient handouts, promotional flyers, and PowerPoint slides.

For insurance-based practices: Each patient will have a face-to-face E/M with you, the provider, while the presentation segment of the Group Visit is being conducted. Each Group Visit lasts 90 minutes from the time patients check in to conclusion and can be conducted at the end of a regularly scheduled business day (4:30-6 p.m.).

**To learn more about Group Visits or to set up an implementation call with one of our Support Team Clinicians, please visit the Lifestyle Matrix Resource Center at LifestyleMatrix.com.**