The Critical Role of Adrenal Hormones in Immunity

with

James L. Wilson ND, PhD
The purpose of this webinar is to help the interested physician understand the basic interactions of steroid hormones with immune function.
Topics We Will Cover

This presentation presents some of the details of the interaction between adrenal hormones and the immune system, including:

- How adrenal hormones affect immunity
- How cortisol and other steroid hormones modify Th1/Th2 function and other outcomes in the immune response
- Clinical presentations of Th1 vs Th2 dominant patients
- Clinical outcomes of hormone/immune interactions in low and high hormone states
- Laboratory tests to monitor key hormone and immune functions
- Clinical interventions you can do to alter and rebalance hormone and immune dysfunction
Introduction
Stress and Disease

"Stress-related disease emerges, predominantly, out of the fact that we so often activate a physiological system that has evolved for responding to acute physical emergencies, but we turn it on for months on end, worrying about mortgages, relationships, and promotions."¹

• States of acute stress, lasting only a few hours may indeed be good for the body, increasing responses to infection, speeding healing, etc. ¹

• But over time with continued stress, the immune system, controlled primarily by the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adrenal medullary (SAM) axis, shift the immune response into aspects of dysregulation.¹

A Brief Review of Lymphocytes

- Lymphocytes all begin in the bone marrow.
- B-lymphocytes mature in the bone marrow and later in lymph glands.
- T-lymphocytes incubate in bone marrow but begin maturing in the thymus, continue maturing in the lymph glands and complete maturation in the site of activation.
Cytokines and Receptors
Cytokines and Receptors

• Cytokines
  – Derived from Greek for “cell movement” (cyto, κύτος“ kytos = cell + kines, "κίνηση" kinisi = movement)
  – Small messenger proteins (~5–20 kDa) by which immune cells communicate with each other
  – Cytokines control much of the immune response.
  – Released from and received by T-lymphocytes

• Receptor sites
  – Areas on cells that receive cytokines, antibodies and other proteins and glycoprotein messengers
Cytokines and Receptors cont.

• The immune system is controlled and identified by cytokines and receptor types.
• All T-cells have CD4 (aka T4) receptor sites.
• Upon binding of a ligand to a receptor, the T-cell is stimulated to take various actions.
T-lymphocyte
Th1/Th2 Immunity
Th1/Th2 Immunity

- There are 2 major types of T-helper cells
  - T helper 1 (Th1)
  - T helper 2 (Th2)
- They act together to control the majority of T-cell immune responses.
- Their actions can be facilitatory, antagonistic or neutralizing.
Th1/Th2 Immunity

- **Th1** is primarily concerned with cellular immunity.
- **Cellular Immunity**
  - “Hand-to-hand-type combat” immune defense
    - Phagocytosis, etc.
  - Responsible for the chief signs of inflammation
  - Acts against difficult infections
    - Viral
    - Strong bacterial
    - Some fungal
  - Involves mostly T-lymphocytes (T-cells)
Th1/Th2 Immunity

- **Th2** is primarily concerned with humoral immunity
- Humoral immunity
  - Artillery-type combat-type immune defense
    - Antibody formation
  - Responsible for most allergic (IgE, IgG_{2,4} reactions)
- Acts against superficial and easier to contain bacterial infections
- Involves mostly B-lymphocytes (B-cells)
Cell-mediated vs. Humoral Immunity

**Cellular Immunity**
- Controlled by cytokines secreted primarily by Th1 cells
- Causes mainly cell-to-cell combat
- Directed primarily by T-lymphocytes

**Humoral Immunity**
- Controlled by cytokines secreted primarily by Th2 cells
- Causes mainly antibody formation
- Directed primarily by B-Lymphocytes
Cellular & Humoral Immunity
How T Cells Differentiate into Th1 and Th2 cells
Th1-Type Immunity
Th1-Type Immunity

• Naïve T-cells (Th0 cells) are exposed to an antigen by a macrophage or other antigen presenting cell (APC).

• In the presence of an abundance of IFN-gamma, or IL-12 cytokines, the Th0 cell “polarizes” (transforms) into a Th1 cell dedicated only to recognizing and responding to the antigen to which it was exposed and has become sensitized.
Th1-Type Immunity

• “Polarized” Th1 cells then continue to “clone” themselves by secreting interleukin-2 (IL-2), which binds to naïve T-cells (Th0) and causes proliferation of the same type of Th1 cell dedicated only to that pathogen.

• Thus creating a small army of Th1 cells dedicated to protecting against a single pathogen.
Th1-Type Immunity
Th1-Type Immunity

From this time forward this Th1 cell secretes IL-2 and IFN-gamma whenever its antigen is present, which causes:

• **Increased production of polarized Th1 clones for that pathogen**
• **An increase in cell-mediated immunity**
  – Increased *macrophage activity*
  – **Chemotaxis** – attracts more polymorphonuclear leukocytes (pmnls), macrophages, killer cells, monocytes and cytotoxic T-cells to the site of injury for hand-to-hand combat
  – **Chemostasis** – keeps more of these same cells at the site of injury
  – **Opsinogen activities** – weakens enemy cells and attracts phagocytic and killer cells, increasing their killing activity
Th1 Cells

T helper 1 (Th1) cells are the principal regulators of type 1 immunity

Mature Th1 cells secrete IL-2, IFN-gamma and lymphotoxin-alpha; aka [tumor necrosis factor-β (TNF-β)]

Whenever you read about IFN-gamma being involved in a reaction, know that this is cellular immunity (T-lymphocytes) stimulating hand-to-hand combat.
IFN-gamma

• **IFN-gamma secreted by**
  – Th1 cells
  – Monocytes
  – Cytotoxic T (CD8) cells
  – Natural Killer (NK) cells & Natural Killer T-Cells (NKT)

• **IFN-gamma is the chief cytokine responsible for producing:**
  – The milieu necessary for Th1 cells to be stimulated and proliferate.
  – The proinflammatory effect
IFN-gamma cont.

• **Stimulates Killing of Microbes**
  
  – Phagocytosis
  – The oxidative burst (hydrogen peroxide and other peroxides, lysozymes and other reactive oxygen species secreted by macrophages, monocytes, etc. under the influence of Th1 cytokines)
  – Antigen presentation to T-cells by several types of cells
  – Other cells to secrete proinflammatory cytokines
  – Direct inhibition of bacterial and viral pathogens
IFN-gamma cont.

- Has special effects on endothelial cells to cause:

A. Endothelial Cell Contraction
   [Image of endothelial cell contraction]
   
   http://ajpheart.physiology.org/content/310/9/H1055

B. Vascular Smooth Muscle Relaxation
   [Image of vascular smooth muscle relaxation]
   
   http://ars.els-cdn.com/content/image/1-s2.0-S1347861315001954-gr1.jpg
IFN-gamma cont.

- This results in:
  - Accumulation of blood in and around dilated, leaky vessels → diapedesis of leukocytes into extravascular (interstitial) sites of “danger”
  - Recruitment of naïve Th0 Cells locally
  - Opsonins into the interstitium
  - Suppresses IL-4 secretions from Th2 cells
IFN-gamma cont.

• Thus, Th1 cells, via IFN-gamma, cause the cardinal signs of inflammation:

RUBOR  TUMOR  CALOR  DOLOR
IL-12

The cytokine IL-12 needs to be present for Th1 polarization and proliferation to occur
Th2-Type Immunity
Th2-Type Immunity

- Naïve T-cells (Th0) cells are **exposed** to an antigen by a macrophage or other antigen presenting cell (APC).

- In the presence of an abundance of IL-4, IL-10 and/or IL-13 cytokines, the Th0 Cell “**polarizes**” into a Th2 cell dedicated only to recognizing and responding to the antigen to which it has been exposed and become sensitized.
Th2-Type Immunity cont.

• “Polarized” Th2 cells then continue to “clone” themselves by secreting IL-4, which binds to naïve T-cells (Th0) and causes proliferation of the same type of dedicated Th2 cell.

• The Th2 cells thus creates **abundant clone Th2 cells** to stimulate B-cells to secrete specific antibodies against a single pathogen.
Th2 Cells

- **IL-4, IL-10 and IL-13 cytokines**
  - *Activate B-cell proliferation* via IL-1, leading to *increasing* B-cell populations in the area
  - *Increase antibody production* (mostly from B-lymphocytes)
  - *Promote class-switching* (switching of the local environment from an IgG to an IgE-predominant environment, etc.)
Th2 Cells cont.
Th2 Cells cont.

- **IL-4, IL-5, IL-9, IL-10 and IL-13**, have all been shown to be strongly associated with **allergic reactions** and **in-airway inflammation**, as seen in **asthma** and **reactive airway disease**.
Th2 Cells cont.

- Type 2-mediated inflammation is characterized by:
  
  - Eosinophilic Inflammation (IgE reaction)
  - Basophilic Tissue Infiltration & degranulation (IgE reaction) Histamine release
  - Mast Cell Degranulation
  - IgG2 and IgG4 Elevation
  - Antibody-Related Reactions
Factors that Cause a Shift to Th1 or Th2 Dominance

- Factors that regulate polarization of newly activated naïve Th0 cells into Th1 or Th2 cells

<table>
<thead>
<tr>
<th>Local Cytokine Milieu</th>
<th>Antigen Dose</th>
<th>Type of Antigen-Presenting Cell Stimulating the Naïve T-Cell</th>
<th>Hormones – Systemic and Local</th>
<th>Local “Danger” Signals</th>
</tr>
</thead>
</table>
The Adrenal Hormones Have Significant Control Over Th1/Th2 Balance
How Hormones Affect Immunity
### Levels of Endocrine Action

<table>
<thead>
<tr>
<th><strong>ENDOCRINE</strong></th>
<th><strong>PARACRINE</strong></th>
<th><strong>AUTOCRINE</strong></th>
<th><strong>INTRACRINE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Produced in one or more parts of the body and act on one or more remote tissues or organs of the body</td>
<td>Produced within one tissue and act on different tissues in the same organ</td>
<td>Produced and act within the same tissue of an organ</td>
<td>Produced and acting within the same cell</td>
</tr>
</tbody>
</table>

---

**How Hormones Affect Immunity**

International © Dr. James L. Wilson, August 1, 2017; All rights reserved. Reproduction prohibited without author's written permission.
How Hormones Affect Immunity cont.

- **TH1 to TH2 Shifts**
  - Systemic hormonal levels set the background for the direction of Th0 cell polarization into either Th1 or Th2 cells.
  - The local hormonal milieu determines the local polarization strategy.
  - Local hormone milieu is, at least partially, controlled by the systemic hormonal milieu.

How Hormones Affect Immunity cont.

• TH2 to TH1 Shifts
  – Hormones that shift immune reactions towards Th1-type reactions

testosterone; dihydrotestosterone

dehydroepiandosterone (DHEA; DHEAS)

androstenedione

How Hormones Affect Immunity cont.

- **TH1 to TH2 Shifts**
  - Hormones that shift immune reactions towards Th2-type reactions:

  - High levels of glucocorticoids
  - Estrogens – especially estradiol, and hydroxylated estrogens 2 and 16
  - Catecholamines (epinephrine and norepinephrine)

Hormones affect the TH1/Th2 outcome

- Elevated glucocorticoids are powerful stimulators of Th2 outcomes by:
  - Directly inducing IL-4 and IL-10 production
  - Suppressing secretion of IFN-gamma, IL-2 and IL-12
    - Suppressing IL-2 inhibits activated T-cells from proliferating and promotes Th2 cell multiplication.

How Hormones Affect Immunity cont.

Hormones affect the TH1/Th2 outcome

• At high concentrations, glucocorticoids
  – Suppresses all lymphocyte proliferation (Th0, Th1 and Th2)
  – Induces lympholysis
  – Inhibits all cytokine secretion (Th1 & Th2)
  – Causes involution and atrophy of the thymus gland

How Hormones Affect Immunity cont.

Hormones affect the TH1/Th2 outcome

• At low glucocorticoid concentrations
  – Lymphocytosis prevails
  – Lack of strong immune response
  – Th1 shifts are prevalent
    • Proinflammatory reactions go unchecked
    • Increase in tissue destruction
    • Increase in production of Th1 dominant cells
  – Overall immunity decreases and recovery from illness is slower

• However, at normal levels of glucocorticoids
  – The Th1/Th2 immune response tends to be balanced & appropriate
Sex hormones seem to play an important role as modulators of autoimmune disease onset/perpetuation. Generally, steroid hormones are implicated in the immune response.

- Estrogens (*especially OHE-2 & OHE-16*) are enhancers, of humoral immunity (Th2).
- Androgens, progesterone and glucocorticoids (*at high levels*) are natural immunosuppressors of Th2.

*Italics mine

Hormones affect the TH1/Th2 outcome

- DHEA
  - Potentiates Interleukin-2 (IL-2) secretion
  - Establishes Th1 clones

How Hormones Affect Immunity  cont.

Th1/Th2 and sex of animal

• Under identical conditions being exposed to the same pathogen:
  – Male animals mount more of a Th1 dominant reaction
  – Females mount more of a Th2 dominant reaction

• This difference is believed to be due to the increased amount of estrogen in females and/or the increased amount of DHEA and testosterone in males

How Hormones Affect Immunity cont.

- **Catecholamines (epinephrine and norepinephrine)**
  - Inhibit Th1 cytokine production (IL-2) and suppress Th1 proliferation (IL-12)
  - Promote Th2 proliferation (IL-1) and Th2 cytokine production (IL-4, IL-10 and IL-13) which perpetuates continued Th2 proliferation
• Stress
  – Increases glucocorticoid production
  – Increases catecholamine production
  – Moderate stress shifts towards a Th2 reaction
  – Makes fighting deep disseminated infections more difficult (because of shift away from a Th1 dominant response)
  – High stress or constant stress may impair the entire immune mechanism – both Th1 and Th2 as well as production, activation and polarization of naïve T-cells.
How Hormones Affect Immunity cont.

• **Chronic Stress**

  – The majority of the stress response, both systemically and locally, is hormone related.

  – Causes almost the complete disappearance of eosinophils and relative lymphopenia (detected on absolute counts of a CBC)

  • This can happen during times of concentrated stress and also during glucocorticoid administration at higher levels.
• Neither up nor down regulation of immunity by hormones is necessarily beneficial or destructive to the host.

• The difference lies in the current status of host immunity, in what direction it needs to move and the amount of suppression or stimulation needed versus what are the present immune challenges.
What Immunity Does to Hormones

• Cytokines influence the activity of hormones locally.
  – Local cytokines greatly influence which hormones will be dominant locally \(^1,^2\);
  – However, even with this predisposition, when Th1 activity becomes too intense locally and threatens the survival of the local cells, IFN-gamma causes activation of the hormone aromatase locally, to increase local estrogen concentrations \(^1\), to cause a switch from a Th1 to a Th2 response to protect the local cells from excessive damage, caused by the aggressive action of Th1 dominant actions.
  – Similarly, androgens can paradoxically inhibit damage to synovial cells of joints by triggering a Th2 response when their concentration becomes sufficiently high\(^2\) preventing excessive damage of synovial membranes when attacking a pathogen within the joint.

Clinical Indicators of Th1/Th2 Dominance
Clinical Differences between Th1 and Th2 Immunity

Th1 dominance

- Clinical - Cardinal signs of inflammation
  - heat,
  - swelling,
  - pain,
  - Redness
  - Most signs of active infection (swelling, pus, suppuration, inflamed tissue, fever, local and systemic flushing)
Clinical Differences between Th1 and Th2 Immunity cont.

**Th2 dominance**

Clinical - Antibody-type reactions more common

- Allergic histamine-type reactions (IgE) more frequent
- Delayed allergic food and environmental reactions (IgG 2,4) more common
- Skin and mucous membrane sensitivities and reactions
- Systemic allergic reactions
- Asthma and obstructive reactive airway reactions common

**LAB TESTS**

- Elevated IgE
- Elevated IgG 2,4
- Elevated IL-1, IL-4 & IL-10
Clinical Differences between
Th1 and Th2 Immunity cont.

• Determining whether it is a Th1 or a Th2 dominant response is often a clinical decision (but if it involves autoimmunity or infection, it is probably a Th1 dominant response).
Salivary Hormone Lab Tests

• Cortisol 4X
• DHEAS
• Testosterone*
• Estrogen*
• Progesterone*
• Estrogen/Progesterone ratio*

* Normal ranges vary between laboratories
Urinary Catecholamine Test

• Epinephrine (Epi)
• Norepinephrine (Norepi)
Other Helpful Lab Tests

- Chem-Panel (Fasting)
- Complete blood count (CBC) with a white blood count differential (diff)
- Eosinophil sedimentation rate (ESR)
- C-reactive protein (CRP)
- 25-hydroxyvitamin D (25 OHD)
- Thyroid test
- Anti-nuclear antibody test (ANA)
Interpretation of Lab Tests
Salivary Hormone Lab Tests Interpretation

• **Cortisol 4X** – Should be within normal limits.
  
  – If salivary cortisol scores are generally low normal or low, Th1 aggressiveness may be limited.
    
    • a strong Th1 response needs adequate cortisol to inhibit the pro-inflammatory results produced by the strong Th1 response needed to kill pathogens.
    
    • The entire immune response may be less than adequate because cortisol is required by all WBCs.
  
  – If cortisol is elevated, the adrenals are probably over-functioning and may cause an unhealthy or premature shift to Th2.

• **DHEAS** – Should be within normal range to help balance Th1/Th2 activity. Slightly elevated for age promotes strong TH1 activity.
  
  – Lack of DHEAS may allow unhealthy shift to Th2.
Salivary Hormone Lab Tests Interpretation cont.

- **Testosterone** – Should be within normal range for age to help balance Th1/Th2 activity.
  - Lack of testosterone may allow unhealthy shift to Th2.
- **Estrogen** – Should be within normal range for age and phase of cycle.
  - If elevated, may cause unhealthy shift to Th2.
- **Progesterone** – Should be well within normal range.
  - If low, may contribute to an unhealthy shift to Th2.
- **Estrogen/Progesterone ratio** – Should be well within normal limits, siding towards progesterone, to help keep healthy Th1/Th2 balance.

* Normal ranges vary between laboratories
Low Adrenal Hormones

- Low adrenal hormones consistently precede the onset of autoimmune diseases (Chronic Th1/Th2 imbalance)
  - Low cortisol → lack of anti-inflammatory override of Th1 response
  - Low Estrogen → lack of modulation of proinflammatory response
  - Low DHEAS → lack of stimulation of virulent Th1 response on first contact with pathogen or non-self cells so pathogens are not fully contained
  - Low Testosterone → same as DHEAS
Urinary Catecholamine Test

• Epi and Norepi should be well within normal limits
  – If the catecholamines are elevated, look for an Th2 dominant response
  • Do we need to consider elevated catecholamines in our therapy?

<table>
<thead>
<tr>
<th>Catecholamine</th>
<th>24-hour urine test range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>0-20 µg/24 hours¹</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>15 to 80 mcg/24 hours (89 to 473 nmol/24 hours) ²</td>
</tr>
</tbody>
</table>

2. [https://medlineplus.gov/ency/article/003613.htm](https://medlineplus.gov/ency/article/003613.htm)
Serum Thyroid Tests
Are thyroid hormone levels sufficient to allow optimal immune function?

- **TSH**
  - Blood spot – range 0.5-3.0 μU/ml\(^1\)
  - Venus draw – range 0.40-2.50 mIU/l\(^2\)
- **Free T4**
  - Blood spot range 0.7-2.5 ng/dl\(^1\)
  - Venus draw range 0.8-1.8 ng/dl\(^3\)
- **Free T3**
  - Blood spot range 2.5-6.5 pg/ml\(^1\)
  - Serum range 2.3-4.2 pg/ml\(^4\)
- **TPO**
  - Blood spot range IU/ml 0-150 (borderline 75-150)\(^1\)
  - Serum range 2.3-4.2 iu/ml\(^5\)

1. Courtesy of ZRT Lab
3. Quest Diagnostics
4. Mayo Medical Laboratories
Thyroid Tests Interpretation cont.

<table>
<thead>
<tr>
<th>Test</th>
<th>(   )</th>
<th>__________</th>
<th>________</th>
<th>(   )</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>(   )</td>
<td>________</td>
<td>________</td>
<td>(   )</td>
</tr>
<tr>
<td>Free T4</td>
<td>(   )</td>
<td>________</td>
<td>________</td>
<td>(   )</td>
</tr>
<tr>
<td>Free T3</td>
<td>(   )</td>
<td>________</td>
<td>________</td>
<td>(   )</td>
</tr>
<tr>
<td>RT3</td>
<td>(   )</td>
<td>________</td>
<td>________</td>
<td>(   )</td>
</tr>
<tr>
<td>TPO</td>
<td>(   )</td>
<td>______</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Serum Vitamin D Lab Tests Interpretation

• Is the 25-hydroxyvitamin D (25 OHD) level optimal for optimal immune function?
  – 75 nmol/l – optimal serum level\(^1\)
  – Less than optimal level (<75 nmol/l) may affect immunity in several ways.\(^2\)
    • check your lab closely

Interpretation of Lab Tests

**Chem-panel (fasting)** - Do we need to do more than just address the Th1/Th2 balance problem?

**CBC+Diff** - Is there an active or chronic viral or bacterial infection?

**ESR, CRP** - Is there an active inflammatory process? If so, how much inflammation/tissue destruction is going on?
Interpretation of Lab Tests

- **IgG1, IgG3, IFN-gamma** – if elevated, indicators of Th1 activity
- **IgE, IgG 2 IgG,4 Epi, Norepi** – if elevated, indicators of Th2 activity
  - When tested over time, is there a Th1/Th2 shift taking place?

Dietary Supplements to Help Th1/Th2 Balance
Adrenal Support

• **Adrenal support** – Returning the adrenals to normal production of their steroid hormones is key to modulating the stress response to beneficially influence the Th1/Th2 balance.

• Hormones of the adrenal cortex that affect Th1/Th2.
  – Cortisol
  – Progesterone
  – DHEA & DHEAS
  – Testosterone
  – Estrogen
  – Androstenedione
Adrenal Support cont.

Glandular Extracts are the cornerstone for adrenal recovery.

• Multi-glandular extracts designed for adrenals
  – The best ones contain adrenal, hypothalamus, pituitary and gonad
  – 4-6 caplets/day for 6 months – up to 2 years
  – Use in conjunction with other treatments.
Adrenal Support cont.

• Vitamin/mineral combination designed specifically to support adrenal hormone production
  – B complex quantities and ratios
    • Niacin (125-150 mg/day) as inositol hexaniacinate
    • B-6 (150 mg/day) – P5’P often better utilized
    • Pantothenic acid (1200-1500 mg/day)
    • Other B vitamins in well-balanced ratios
  – Trace minerals in the proportion they are needed for the adrenal cascade
Adrenal Support cont.

- **Vitamin C 2,000-5,000 mg/day (such as Adrenal C)**
  - 1:2 ratio of bioflavonoids to vitamin C
  - pH balanced
  - Sustained release
  - Trace minerals used in the adrenal cascade (Zn, Mg, Mn, Cu)
  - The adrenals use more vitamin C than any other organ or gland.
  - Vitamin C is needed to overcome inflammatory reactions and heal damaged tissue
Adrenal Support cont.

- **Herbal Remedies used in combination to balance the HPA axis**
  - **Licorice (Glycyrrhiza glabra)**, a specific for adrenal fatigue
    - Do not exceed 1/4 lb/day to avoid increase in blood pressure (BP)
    - Contraindicated in cases of hypertension if BP rises upon ingestion
  - **Ashwagandha (Withania somnifera)**
  - **Maca (Lepidium meyenii)**
  - **Eleuthero (Eleutherococcus senticosus)**
  - **Korean Ginseng (Panax ginseng) [for men]**
Adrenal Support cont.

• Magnesium citrate or glycinate
  – 400 mg before bedtime
  – 200-400 mg during the day, if needed
Adrenal Support cont.

Adrenal Hormone Precursors

- **Pregnenolone**
  - 150 mg micronized, time released/day
  - Signs of excess – acne and facial hair usually first signs of excess
Thyroid support

- Multivitamin/mineral formula in an easily absorbed form
  - Liquid minerals and nutrients for the thyroid
    - High in inorganic iodine
    - High in tyrosine
  - Trace minerals – water soluble is best
    - Selenium
    - Zinc
    - Other trace minerals
• T-helper Lymphocytes of the immune system respond to pathogens via either a Th1 or a Th2 dominant reaction.
• This reaction can be local and/or systemic.
• A Th1 response is produced by T-lymphocytes and is initiated to kill strong bacterial, viral and fungal pathogens.
• A Th2 response is produced by B-lymphocytes and is initiated to kill weaker pathogens or to weaken strong pathogens.
• Th1 responses produce IFN-gamma and TNF-β, which increase phagocytosis, chemotaxis, chemostasis and opsinogen activities to contain and kill pathogens.

• Its action is mainly cell-to-cell contact, producing the classic clinical symptoms of inflammation: rubor, tumor, calor, dolor.

• Laboratory tests to confirm an increase in systemic Th1 activity increases IFN-gamma, IgG1,3, IL-2 and IL-12.
• Th2 responses produce IL-1,4,10,13, which increase antibody production to specific pathogens.

• Its action is mainly an antibody response, producing the clinical symptoms of inflammation and allergic reactions.

• Laboratory tests to confirm an increase in systemic Th2 activity are increased IgE, IgG2,4, and IL-1,4,10.
• Androgenic hormones – DHEA, testosterone, androstenedione and probably progesterone influence a shift towards a Th1 response.

• Estrogenic hormones (especially hydroxylated estrogens 4 and 16) and catecholamines influence a shift towards a Th2 response.
Glucocorticoids act in different ways depending upon their local and circulating levels:

- Elevated glucocorticoids shift the immune reaction towards a Th2 response to protect the host from tissue destruction that could result from an overly active Th1 response.

- Decreased glucocorticoids shift the immune reactions towards a Th2 response because low cortisol levels cannot protect the cells from the strong inflammation and tissue destruction caused by a Th1 response.
Normal glucocorticoid levels, with their strong anti-inflammatory properties, protect cells from the excess destruction of a strong Th1 response, allowing the cell-to-cell combat to eradicate the pathogen without undue harm to tissues.
Stress plays a deciding role in many Th1/Th2 shifts, elevating catecholamines and glucocorticoids.

As the overall stress load increases or becomes chronic, the likelihood increases of a strong Th1 response turning into a weaker Th2 response.

This saves the host from the strong Th1 response but allows the pathogen to live, forming the basis for many autoimmune reactions.
Specific dietary supplements have been successfully used to help shift the Th1/Th2 response towards a better hormone balance and more appropriate immune response to stress.
Phone: 1-888-ADRENAL (888-237-3625)
Fax: 520-514-1917
E-mail: drwilson@icahealth.com

www.adrenalfatigue.org
www.icahealth.com  (practitioner only)
THANK YOU!

James L. Wilson ND. PhD