A Basic Introduction to RNA

Dr. Amy A. Yasko
RNA

- Diagnostic tools
- Drugs
- Nutritional supplements
- Homeopathic drugs
- Medical foods
We have the same unique DNA in every cell in our body.
IF the IDENTICAL genetic information is in every cell in the body, what determines how different cells differentiate?
RNA
RNA has the ability to direct the synthesis of proteins

- Heart Disease **CRP**
- Cholesterol Metabolism **HMGCoA**
- Weight Management **Leptin**
- Inflammation **IL6, COX2, LO**
By **MODULATING** the levels of RNA, one has the ability to **SPECIFICALLY** affect the levels of **ANY** protein in the body.
One way to think about regulations of functions within the body, is as a series of gauges each of which controls a different function in the body. When everything is in balance, the dials on the gauges are in the middle of their range, as in the upper left hand square. However, anyone of these gauges can be out of balance at any given time as depicted in the other three squares; the “needle” on the gauges can be too high or too low, and any one of the gauges may malfunction. By using individual RNA NutriSwitch Formulas, it is possible to rebalance any individual gauge. The RNA that it would take to balance the upper right hand square is different from the RNA that it would take to balance the lower left hand square. Yet another RNA would be necessary to balance the lower right hand square. There are hundreds of reactions or functions going on in the body at any moment, and any one of these myriad functions can go wrong in a variety of ways. It is easy to understand how an individual may need one, or one hundred different RNA NutriSwitch Formulas in order for all of his or her “gauges” to be balanced. Using this analogy it is also easy to see why using specific NutriSwitch Formulas is a distinct advantage over using a total RNA Supplement. If we use the upper right square as an example, only one gauge is out of balance. It makes more sense to use an RNA that will help to balance that particular gauge, rather than simply throwing all of the different RNAs at it and hoping that one of them will help to balance that gauge.
A very specific example of a “gauge” in the body getting out of balance that we are all familiar with is the body’s temperature gauge. Normally the body will allow the temperature to fluctuate below 98.6 degrees, as well as to go above 98.6 degrees, and it is still able to control the temperature. However, if the fever gets too high, i.e. above 105-106 degrees, the body loses its ability to self regulate, and it can be necessary to put an individual into an ice water bath to physically bring down the temperature and get that gauge back in balance. Conversely, if a person's body temperature drops too low, as in hypothermia, it is necessary to physically warm the individual and bring their temperature back up manually, as the body has lost the ability to do it on its own. There are a multitude of functions that can get so out of balance that the body loses the ability to self regulate. These are cases when we use specific RNA NutriSwitch Formulas to help get those individual functions back into balance.

Many of us have had the experience of having the needle on an analog gauge get “stuck”. All that is necessary to get it loose is to smack the gauge on the side and the needle will move freely again. The most simplistic way to look at using RNA NutriSwitch formulas is that they help to “smack” the side of the gauge and free the needle so that everything can once again be in balance.
NATURALLY Occurring Regulatory Process

- Plants
- Bacteria
- Animals
HUMANS TYPICALLY EAT SEVERAL GRAMS OF NUCLEOTIDES IN THEIR DIET EACH DAY
<table>
<thead>
<tr>
<th></th>
<th>Adenine (mg/10 g)</th>
<th>Guanine (mg/100 g)</th>
<th>Hypoxanthine (mg/100 g)</th>
<th>Xanthine (mg/100 g)</th>
<th>Total purines (mg/100 g)</th>
<th>RNA (mg/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ Meats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beef liver</td>
<td>62</td>
<td>74</td>
<td>61</td>
<td>0</td>
<td>197</td>
<td>268</td>
</tr>
<tr>
<td>Beef kidney</td>
<td>42</td>
<td>47</td>
<td>63</td>
<td>61</td>
<td>213</td>
<td>134</td>
</tr>
<tr>
<td>Beef heart</td>
<td>15</td>
<td>16</td>
<td>38</td>
<td>102</td>
<td>171</td>
<td>49</td>
</tr>
<tr>
<td>Beef brain</td>
<td>12</td>
<td>12</td>
<td>26</td>
<td>112</td>
<td>162</td>
<td>61</td>
</tr>
<tr>
<td>Pork liver</td>
<td>59</td>
<td>77</td>
<td>71</td>
<td>82</td>
<td>289</td>
<td>259</td>
</tr>
<tr>
<td>Chicken liver</td>
<td>72</td>
<td>78</td>
<td>71</td>
<td>22</td>
<td>243</td>
<td>402</td>
</tr>
<tr>
<td>Chicken heart</td>
<td>32</td>
<td>41</td>
<td>12</td>
<td>138</td>
<td>223</td>
<td>187</td>
</tr>
<tr>
<td><strong>Fresh seafood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anchovies</td>
<td>8</td>
<td>185</td>
<td>6</td>
<td>212</td>
<td>411</td>
<td>341</td>
</tr>
<tr>
<td>Clams</td>
<td>14</td>
<td>24</td>
<td>12</td>
<td>86</td>
<td>136</td>
<td>85</td>
</tr>
<tr>
<td>Mackerel</td>
<td>11</td>
<td>26</td>
<td>5</td>
<td>152</td>
<td>194</td>
<td>203</td>
</tr>
<tr>
<td>Salmon</td>
<td>26</td>
<td>80</td>
<td>11</td>
<td>133</td>
<td>250</td>
<td>289</td>
</tr>
<tr>
<td>Sardines</td>
<td>6</td>
<td>118</td>
<td>6</td>
<td>215</td>
<td>345</td>
<td>343</td>
</tr>
<tr>
<td>Squid</td>
<td>18</td>
<td>15</td>
<td>24</td>
<td>78</td>
<td>135</td>
<td>100</td>
</tr>
<tr>
<td><strong>Dried legumes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garbanza bean</td>
<td>17</td>
<td>14</td>
<td>18</td>
<td>7</td>
<td>56</td>
<td>356</td>
</tr>
<tr>
<td>Split peas</td>
<td>88</td>
<td>74</td>
<td>11</td>
<td>22</td>
<td>195</td>
<td>173</td>
</tr>
<tr>
<td>Lentils</td>
<td>54</td>
<td>51</td>
<td>15</td>
<td>42</td>
<td>162</td>
<td>140</td>
</tr>
<tr>
<td>Blackeye peas</td>
<td>104</td>
<td>82</td>
<td>20</td>
<td>16</td>
<td>222</td>
<td>306</td>
</tr>
<tr>
<td>Pinto bean</td>
<td>46</td>
<td>39</td>
<td>25</td>
<td>34</td>
<td>144</td>
<td>485</td>
</tr>
</tbody>
</table>
Breast milk has been reported to contain 1-12 mg/dL of DNA and 10-60 mg/dL of RNA.

broken down into components
- Nucleotides
- Ribose
RNA

Components or Nucleotides

- purines
- pyrimidines

adenine

guanine

cytosine

uracil ($R=H$)
thymine ($R=CH_3$)
RNA Nucleotides

Natural RNA (or DNA)
broken down

Nucleotides
Purines & Pyrimidines
+ Ribose

Allopathic Use of RNA

Synthetic RNA (or DNA)
Does not break down
Oligonucleotide Backbone Modification

- Phosphodiester
- Phosphorothioate
- Methylphosphonate
<table>
<thead>
<tr>
<th>First generation</th>
<th>Second generation</th>
<th>Third generation</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Phosphorothioate DNA (PS)" /></td>
<td><img src="image" alt="2'-O-methyl RNA (OME)" /></td>
<td><img src="image" alt="2'-O-methoxy-ethyl RNA (MOE)" /></td>
</tr>
<tr>
<td><img src="image" alt="Peptide nucleic acid (PNA)" /></td>
<td><img src="image" alt="N3'-P5' Phosphoroamidate (NP)" /></td>
<td><img src="image" alt="2'-fluoro-arabino nucleic acid (FANA)" /></td>
</tr>
<tr>
<td><img src="image" alt="Locked nucleic acid (LNA)" /></td>
<td><img src="image" alt="Morpholino phosphoroamidate (MF)" /></td>
<td><img src="image" alt="Cyclohexene nucleic acid (CeNA)" /></td>
</tr>
</tbody>
</table>
Synthetic, modified RNA (DNA) $\rightarrow$ drugs

Natural, unmodified RNA (DNA) $\rightarrow$ GRAS
Nucleotides as non-essential nutrients

• For years, nucleotides were not considered essential nutrients

• It was thought de novo synthesis of nucleotides was sufficient
“Dietary sources of nucleotides appear important to support optimal growth and function of metabolically active cells such as lymphocytes, macrophages and intestinal cells. This requirement is evident only with stress, such as an immune challenge, major tissue injury, systemic infection or early infancy and spurt growth of adolescence. Although all nucleotides do not appear to have an equal effect, a mix of all nucleotides seems to provide the most complete response. Nucleotides are now being used commercially as feed additives to improve animal growth or disease resistance.”

Nucleotides serve as precursors for nucleic acid synthesis, participate in energy transfer reactions, and function as coenzymes. Dietary purines and pyrimidines in nucleic acids are absorbed mainly in the form of nucleosides and bases. Gastrointestinal and liver tissues metabolize dietary nucleotides extensively prior to their entry into the systemic circulation. The endogenous supply of nucleotides is maintained both through de novo synthesis and through salvage pathways in which purines and pyrimidine bases and nucleosides are converted to nucleotides.

“Nucleotides participate in several biochemical processes that are essential to the function of the living body.

• As nucleic acids: being the monomeric units they carry the genetic code as DNA and RNA

• In biosynthesis: for example, UDP-galactose in the synthesis of lactose or UDP-glucose in the process of glycogenesis

• As components of co-enzymes: NAD, FAD and co-enzyme A

• As biological regulators: cyclic AMP initiates second-messenger cascades and is ubiquitous in all forms of life, playing a key role in regulating biological processes

• As an energy source: ATP is a universal currency of energy in biological systems.”

_Nucleotides in Infant Nutrition: A Must or an Option, Aaron Lerner and Raanan Shamir_
The term conditionally essential has been used to describe the role of dietary nucleotides in human nutrition. These nutrients may become essential when the endogenous supply is insufficient for normal function, even though their absence from the diet does not lead to a classic clinical deficiency syndrome. Conditions under which these nutrients may become essential include certain disease states, periods of limited nutrient intake or rapid growth, individuals at increased risk of acquired infection, and the presence of regulatory or developmental factors, which interfere with full expression of endogenous synthetic capacity. Certain tissues including lymphocytes, the gastrointestinal tract, the liver and the brain may have a limited capacity for the salvage and de novo synthesis of nucleotides.


Nucleotides Requirements

• Bone marrow cells, lymphocytes, erythrocytes and some brain cells cannot synthesize some purines (A, G)

• Intestinal mucosa cells cannot make enough purines to fulfill the body’s requirement

• Stress increases the need for nucleotides to overcome negative effects of hormones released during stress.

• Cell repair after injury increases the need for nucleotides.

• The brain has the highest concentration of RNA in the body, and therefore has the highest requirement of RNA.
Nucleotides Requirements

• For an organism to live, it must create new cells as fast as cells die. This means that the body needs to make millions of cells every minute, relying on DNA and RNA.

• This requires an ENORMOUS number of nucleotides JUST to maintain the status quo.; normal DNA contains $3 \times 10^9$ nucleotides.

• RNA is even more abundant than DNA, making the requirement for RNA even greater.

• It is less costly for an organism to use preformed nucleotides of dietary or endogenous origin than to synthesize them de novo.
Panel A. Human Liver Total RNA; 28S:18S rRNA = 1.42

Panel B. Human Heart Total RNA; 28S:18S rRNA = 1.54
Panel D. Human Lung Total RNA; 28S:18S rRNA = 1.48

Panel F. Human Prostate Total RNA; 28S:18S rRNA = 1.95
Functions of Nucleotides (RNA/DNA)

- Multiplication of DNA for cell growth/division
- Direct protein synthesis: mRNA, rRNA, tRNA
- Regulatory Functions: small RNA
- Energy Transport: ATP (adenosine)
- Enzymatic Function:
  - coenzyme A
  - NAD
  - FAD
- Regulatory molecules:
  - cAMP (adenosine)
  - cGMP (guanosine)
There is a tremendous amount of literature to support the use of dietary nutrients showing effects on the intestine, liver, lipid metabolism, immune system, humoral immunity, cellular immunity, resistance to pathogens, energy, detoxification, stress…
RNA Nucleotides

- The concept of the body requiring dietary nucleotides when “under stress”, or “limited nutrients” or “rapid growth” conditions could easily comprise many, if not all, of the chronic conditions that plague us today.
According to the 1999 FDA Dietary Supplement Industry Report:

“Nucleic acids: large molecules that are encoded with genetic instructions… and the oral tablet and capsule forms are non-toxic.”
According to the FDA, “Introduced nucleic acids, in and of themselves, **do not raise safety concerns**. Thus, for example, the introduction of a gene encoding an anti-sense ribonucleic acid (RNA) would not raise concerns about either the gene or the anti-sense RNA. Any safety considerations would focus on the intended effects of the anti-sense RNA. Hence, continuing the example, if the anti-sense RNA were used to suppress an enzyme, then just as for any other method intended to suppress an enzyme, such as deletion or nonsense mutation, the metabolic effects on the host plant of such enzyme suppression should be considered at the conceptual stage of development and monitored, when appropriate and feasible.” …
...Furthermore, the Working Policy states that even the transfer of genetic material in the form of nucleic acids is not subject to FDCA Section 409 because “nucleic acids are present in the cells of every living organism, including every plant and animal.” Nucleic acids that are expressed in GRAS microbes, such as yeast are also GRAS.

Department of HHS FDA Docket No. 92N-0139.
FSHN 101 Food Biotechnology.
Mechanism of Action of RNA

MOLECULE- RNA
Nucleotides as Drugs
for Drug Discovery
as Food
as Nutritional Supp.
as Homeopathics

Mechanism Antisense RNAi Unknown Unknown

Molecule modified RNA ds (or hairpin) RNA natural RNA natural RNA natural RNA
Nucleotides as Drugs

- Antisense Mechanism (naturally occurring mechanism)

- Modified Nucleotide Backbone
  - Prevent Degradation

- Toxicity Issues at High Doses

- Extremely Costly
  - $500,000,000 to regulate a single RNA
RNA Interference

- Naturally occurring mechanism
- Requires synthetic double stranded or hairpin RNA to prevent degradation
- Delivery is an issue
- Costly
- Experimental
Homeopathic RNA

- HPUS Monograph 1971
- Wide variety of health conditions
- Use of Homeopathic RNA for Viral Infections
HPUS RNA

Allergic conditions, cancerous conditions, cortical and medullary hypoasthenia, epilepsy, slowness at school, hypothyroidism, psychological and physical slowness, personality disorders in children, mental over-exertion, acrid dyspepsia, biliary sycosis, entero-pancreatic syndrome, leucopenia, hypotension, arthralgia, lymphoedema, chronic eczema, varicose ulcers.
HPUS DNA

Allergic conditions, cancerous conditions, premature senescence, neurosis from anguish, personality neurosis, narcissistic neurosis, manic depressive psychosis, all mental disorders, ophthalmic migraine, insomnia, anorexia, gingivitis, hyperthyroidism, biliary sycosis, disorders of the liver, disorders of the pancreas, leucopenia, hemorrhage, angina, sinusitis, myopia, conjunctivitis, fractures, burns, alopecia.
Allopathic Approaches to Nucleotides

- Focus on mechanism of action
- Drug development or target validation
- Modified backbones prevent degradation
- Delivery issues
- High doses, toxicity
- Expensive
Alternative Approaches to Nucleotides

- **Medical Food**: required nutrient
  - Substantial literature supports use
  - Mechanism unknown
  - No toxicity, GRAS
  - Inexpensive
  - No delivery issues

- **Nutritional Supplement**: 
  - Substantial literature supports use
  - Mechanism unknown
  - No toxicity, GRAS
  - Inexpensive
  - No delivery issues

- **Homeopathic Drug**
  - Disease conditions in HPUS for DNA/RNA
Case Studies

“One comment about anecdotal evidence: the scientific purists frequently discount such ‘evidence’ as unscientific. This is so even when such cases are being reported world-wide and by different observers. And, indeed, one should approach such cases with a critical, but not, skeptical eye. Many of our medical and scientific discoveries began as anecdotal observations. What distinguished the innovators and the great men of science from their less well known peers was the ability and willingness of the former to accept anecdotal observations as valid, or at least as a starting point. Today, the scientific elitists are too quick to dismiss such accounts out-of-hand without so much as a moment’s consideration. This is poor science.”

Dr. Russell Blaylock, Excitotoxins: The Taste That Kills.
Case Study #1

43 yr. old Male, E.Y.
History of Hyperlipidemia
Case Study #2

46 yr. old Male, D.C.
History of Kidney Disease and Hyperlipidemia
Liver/Pancreas

Cholesterol
Case Study #3

68 yr. old Male, F.R.
Blood Sugar/ Cholesterol Issues
Kidney

Start Kidney Nucleotides

Triglycerides

[Graph showing kidney nucleotide levels from 9/7/01 to 8/10/04]
Case Study #4

26 month old Female, S.H.
Nieman Pick Type A
Fatal Lysosomal Storage Disorder
Deficiency of Acid Sphingomyelinase
Nerves/Excitotoxins

Seizure Activity

Start Nucleotides 2x/day

Go to Nucleotides 3x/day

Go to Nucleotides 4x/day

Avg. # Seizures/Day

Start dates:
- 6/7-6/13
- 6/14-6/20
- 6/21-6/27
- 6/28-7/4
- 7/5-7/11
- 7/12-7/18
- 7/20-7/25
- 7/26-8/2
- 8/3-8/9
- 8/10-8/16
- 8/17-8/23
- 8/24-8/30
- 8/31-9/6
- 9/7-9/13
- 9/14-9/20
- 9/21-9/27
- 9/28-10/4
- 10/5-10/11
- 10/12-10/18
- 10/19-10/25
- 10/26-11/1
- 11/2-11/8
- 11/9-11/13
- 11/13-11/21
- 12/1-12/7
- 12/8-12/14
- 12/15-12/22
- 12/23-12/29
- 12/30-1/6
- 1/7-1/13
- 1/14-1/20
- 1/21-1/27
- 1/28-1/31
- 2/1-2/7
- 2/8-2/14
- 2/15-2/21
- 2/22-2/28
- 3/7-3/13
- 3/14-3/23
- 3/24-3/31

Kidney

Start Kidney Nucleotides
Case Study #5

66 yr. old Male, L.B.
Prostate Issues
Prostate +

Start Prostate + Nucleotides

PSA
Case Study #6

75 yr. old Male, G.W.
Prostate Cancer
Case Study #7

6 yr. old Male, M.W.
Leaky Gut/Malabsorption
One month after starting Bowel Balancing Formula and Stomach pH Balancing Formula
Stress

MAP38K  IL-6

Inflammation
IL-6 May be Stress-Health Link

You don't need research to tell you that stress can make you sick. However, a new study may have discovered the link between stress and health – interleukin-6 (IL-6).¹

IL-6 is a proinflammatory cytokine (small protein released by cells) that directly affects the behavior of other cells in the body. It is associated with many diseases, including arthritis, cancer, diabetes, osteoporosis, Alzheimer's dementia, periodontal disease and cardiovascular disease. IL-6 has also been linked to frailty and functional decline in old age.

Perhaps one of the most important concerns about IL-6 is that it is directly linked to cardiovascular disease. This is due, at least in part, to the fact that it plays a central role in promoting the production of C-reactive protein (CRP), a marker of inflammation that, when elevated, is a significant risk factor for older adults, accelerating host of age-related diseases."³

It is important to note that research has shown that poor habits can also raise levels of IL-6 and includes smoking, lack of exercise, and eating too much alcohol. These findings suggest that reducing stress is important for a healthy lifestyle is imperative. "²

"The bad news is that we are experiencing chronic stress, caregiving or another difficult situation, but we need to be aware that the symptoms may impact your health," author Dr. Ronald Glaser, director of the Institute for Behavioral Research at the Ohio State University, told Life magazine.

"The good news is you can do something about it by changing your habits," said Dr. Glaser. "You can start by taking control of your stress levels. One way to do this is to focus on the positive aspects of your life. This could include spending time with friends and family, engaging in physical activity, or practicing meditation. Additionally, you can take steps to reduce your exposure to stressors, such as limiting your exposure to news and social media. By taking these steps, you can improve your overall health and reduce your risk of developing age-related diseases. "²
Psychology

Chronic stress and age-related increases in the proinflammatory cytokine IL-6


Departments of Psychiatry, Internal Medicine, and Molecular Virology, Immunology, and Medical Genetics, Ohio State University College of Medicine, Columbus, OH 43210; and Department of Psychology, Institute for Behavioral Medicine Research, and Comprehensive Cancer Center, Ohio State University, Columbus, OH 43210; and Department of Psychology, University of North Carolina, Chapel Hill, NC 27599

Edited by Burton H. Singer, Princeton University, Princeton, NJ and approved June 3, 2003 (received for review April 2, 2003)

Abstract

Overproduction of IL-6, a proinflammatory cytokine, is associated with a spectrum of age-related conditions including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, certain cancers, periodontal disease, frailty, and functional decline. To describe the pattern of change in IL-6 over 6 years among older adults undergoing a chronic stressor, this longitudinal community study assessed the relationship between chronic stress and IL-6 production in 119 men and women...
Chronic Inflammation
The Epidemic Disease of Aging

Why do aging people suffer from so many seemingly unrelated disorders? Mainstream medicine attributes these multiple diseases to old age and fails to adequately address them. The sad fact is that people are needlessly suffering and dying from a common problem that is easily correctable.

In what will soon become a medical breakthrough, Life Extension has identified a reversible culprit (systemic inflammation) that is involved in the development of age-related diseases.

This role of inflammation has been overlooked by the medical establishment, yet persuasive scientific evidence exists that correcting a chronic inflammatory disorder will enable many of the infirmities of aging to be prevented or reversed.

Conventional doctors often tell their patients to accept the fact that they are not young anymore. Now that we know that systemic inflammation is a prime reason for the development of degenerative disease, safe steps can be taken to suppress the inflammatory cascade that destroys cells throughout the aging body.

Aging and inflammation
Chronic inflammation inflicts devastating effects, especially as humans grow older. The pathological consequences of inflammation are fully documented in the medical literature. Regrettably, the dangers of systemic inflammation continue to be ignored, even though proven ways exist to reverse this process.

Many people join The Life Extension Foundation (LEF) because they suffer from various degenerative diseases. A common culprit we find in these frail individuals is systemic inflammation.
How worms tackle stress

JNK and p38 pathways are used and integrated in response to pathogen stress in C. elegans
By David Secko
July 14, 2004

When an animal cell encounters a bacterial or chemical toxin, it needs to respond to ensure its survival, but how it does this is still poorly understood. Now, two independent studies clarify the involvement of the c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) signalling pathways in these responses in Caenorhabditis elegans.

Both JNK and p38 are well known mediators of stress responses in mammalian cells, and in C. elegans, these proteins, other components involved in their signalling pathways, and their involvement in stress responses are conserved. The two new papers, reported in the July 12 issue of PNAS, together reveal an evolutionarily interconnected mechanism for responding to bacterial stress.
Diseases Related To Chronic Inflammation

Seemingly unrelated diseases have a common link. People suffering from multiple degenerative disorders often exhibit excess levels of pro-inflammatory markers in their blood. Here is a partial list of common medical problems associated with chronic inflammation:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Chronic inflammation causes most cancers</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>Chronic inflammation contributes to coronary atherosclerosis</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>Chronic inflammation destroys brain cells</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>Chronic inflammation causes heart muscle wasting</td>
</tr>
<tr>
<td>Stroke</td>
<td>Chronic inflammation promotes thromboembolic events</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Inflammatory cytokines destroy joint cartilage and synovial fluid</td>
</tr>
<tr>
<td>Aortic Valve Stenosis</td>
<td>Chronic inflammation damages heart valves</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>Inflammatory cytokines restrict circulation and damage nephrons</td>
</tr>
<tr>
<td>Lupus (SLE)</td>
<td>Inflammatory cytokines induce an autoimmune attack</td>
</tr>
<tr>
<td>Asthma</td>
<td>Inflammatory cytokines close the airways</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Inflammatory cytokines induce dermatitis</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Inflammatory cytokines induced pancreatic cell injury</td>
</tr>
<tr>
<td>Allergy</td>
<td>Inflammatory cytokines induce autoimmune reactions</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Inflammatory cytokines attack traumatized tissue</td>
</tr>
<tr>
<td>Surgical complications</td>
<td>Inflammatory cytokines prevent healing</td>
</tr>
<tr>
<td>Anemia</td>
<td>Inflammatory cytokines attack erythropoietin production</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Inflammatory cytokines are elevated in fibromyalgia patients</td>
</tr>
</tbody>
</table>
Inflammation, Hypertension, and the Metabolic Syndrome

Scott M. Grundy, MD, PhD

In this issue of The Journal, Sesso and colleagues report a positive relationship between increased serum levels of C-reactive protein and the risk for development of incident hypertension in participants of the Women’s Health Study. A total of 20525 women were followed up prospectively for a median of 7.8 years, during which time approximately one fourth of the women acquired elevated blood pressure; those with higher levels of C-reactive protein were more likely to develop hypertension. C-reactive protein levels in the upper ranges of the normal distribution (high-normal levels of C-reactive protein) are widely believed to reflect a state of low-grade chronic inflammation; therefore, the association between higher C-reactive protein levels and new-onset hypertension led Sesso et al to suggest that hypertension may be an inflammatory disease.

The term inflammation is applied by Sesso et al because higher levels of C-reactive protein are thought to result from activation of cells characteristic of an inflammatory response (ie, cells of the immune system and vascular endothelium). Although the response denoted by high-normal levels of C-reactive protein is of a very low-grade chronic nature, it is well recognized that high-normal levels of C-reactive protein are common in persons with the metabolic syndrome, thereby leading to inclusion of a proinflammatory state as one of the syndrome’s components.

Sesso et al did not specifically address the question of what proportion of individuals with high-normal levels of C-reactive protein actually met criteria for the metabolic syndrome. A previous report from their laboratory showed the proportion to be high. Some investigators have questioned whether elevated blood pressure truly is a component of the metabolic syndrome because blood pressure is known to be increased by several nonmetabolic factors (eg, increasing arterial stiffness with aging). Nonetheless, the present demonstration of an apparent connection between low-grade inflammation and hypertension supports the concept that elevated blood pressure should be listed as one of the components of the metabolic syndrome.

Obesity is one of the major underlying causes of the metabolic syndrome. The mechanisms whereby obesity elicits or worsens metabolic risk factors are not fully understood but several potential links exist. Obesity is accompanied by high plasma levels of nonesterified fatty acids that cause insulin resistance in skeletal muscle and overload the liver with lipid.
THE SECRET KILLER

- The surprising link between INFLAMMATION and HEART ATTACKS, CANCER, ALZHEIMER'S and other diseases
- What you can do to fight it
too plump
AN INFLAMMATORY SURPRISE
INFLAMMATION VERSUS THE BRAIN

Evidence mounts that inflammation is involved in neurodegenerative diseases. Chronic inflammation is getting a bad name for its presumed role in several diseases—and new research shows that its notoriety may be well deserved.

A team led by Jeffery W. Kelly, a chemistry professor at Scripps Research Institute, suggests that abnormal cholesterol and lipid metabolites produced as a result of inflammation bond with normal amyloid β peptides in the brain. These reactions increase the peptides’ hydrophobicity, predisposing them to misfold. The misfolded peptides then aggregate into the neurotoxic fibrils characteristic of Alzheimer disease [Proc. Natl. Acad. Sci. USA 2004, 101, 15025-15030].

The inflammatory process involves several types of cells and signaling compounds in a complicated cascade. In the peripheral nervous system, one control point for the cascade centers on the binding of acetylcholine to macrophages, which curtails the cells’ inflammatory response. Last year, Kevin J. Tracey and colleagues at the North Shore Long Island Jewish Research Institute in Manhasset, N.Y., identified the binding...
Case Study #8

57 yr. old Female, A.F.
Polymyalgia Rheumatica
Initial CRP = 14
Prednisone = 15mg

Start Inflammation + Nucleotides

Allergy Nucleotides

CRP < 0.2
Prednisone = 0.5mg
RNA as Drugs, Nutritional Supplements, and Food

Dr. Amy A. Yasko

April 2004
Literature Supporting the Use of Dietary Nucleotides

Dr. Garry Gordon
MD, DO, MPH

April 2004