Introduction

Without restful sleep, health cannot prevail.\textsuperscript{1-3} Healthy sleep is a rapidly reversible behavioral and physiological state that is characterized by partial environmental disengagement and variable unresponsiveness. On the one hand, sleep is often perceived inappropriately as an inactive retirement from consciousness. On the other hand, it is an active physiological state where major changes occur in body metabolism and organ function\textsuperscript{1-7}. Sleep is part of “biorhythms” where the body retires so that it can tend to its recuperative activities\textsuperscript{1-7}.

Scientists toil with attempts to explain the function of sleep, but it is known that sleep is essential for life. Complete sleep deprivation results in rapid death in laboratory animals and significant insomnia produces a litany of pathophysiological changes\textsuperscript{1,3}. Sleep deprivation is a disease promoter with premature aging consequences\textsuperscript{6}. The objective of this article is to review the consequences and clinical management of sleeplessness by natural means. This work has some degree of dissonance with allopathic treatments for insomnia. It is part of the author’s concept of “The Sleep Naturally Plan.”\textsuperscript{1}

The Magnitude of Sleep Problems

I believe that the inappropriate use of prescription or over the counter drugs is a major public health concern\textsuperscript{1}. Although one third of our lifetime is spent dozing or sleeping, scientific studies of sleep have emerged only in the past 50 years or so. Failure to initiate sleep, stay asleep and obtain good quality sleep is the common components of insomnia. When insomnia is defined by strict criteria (sleep disturbance for greater than two weeks), it is apparent that about 10 to 20\% of adults are afflicted\textsuperscript{8-10}. Expert panels of scientists estimate that about one in three (30\%) of the population experiences sleep...
disruption and one in ten (10%) reports daytime symptoms that are associated with insomnia.\textsuperscript{11} I believe that these are conservative estimates.

The magnitude of sleeplessness is greater in the elderly\textsuperscript{1,3}. Sleep “characteristics” change with age but several factors operate in the elderly, including: poor sleep hygiene, inactivity, bereavements, sociobehavioral problems and coexisting diseases, including medical and psychiatric problems\textsuperscript{6}. The prevalence of sleep disorders often underestimated in primary care practice where may individuals with insomnia do not tend to raise their complaints of insomnia\textsuperscript{4}.

About 50\% of all adults attending a primary care physician report insomnia on direct questioning but only a third of this very large clinical population mention their complaints to an examining physician\textsuperscript{5}. Sleep disorders constitute one of several “hidden epidemics” in clinical practice. These occult public health problems include: hypertension, alcohol abuse, sexual dysfunction and Metabolic Syndrome X. It is notable that these “hidden” clinical problems may aggregate in the insomniacs\textsuperscript{1,3}.

**Sleep 101: A Brief Overview**

Sleep cycles are quite dynamic with phases that include rapid eye movement (REM) or non-rapid eye movement sleep (NREM)\textsuperscript{12-14}. The NREM phases vary by deepness of sleep (Stages 1 through 4) and REM is a unique phase\textsuperscript{1,3}. Sleep–wake rhythms are bimodal. During wakefulness the brain exhibits desynchronized wares of low amplitude on electroencephalogram EEG recordings\textsuperscript{1,3,12-14}. In NREM sleep the EEG shows synchronized, progressively slower waves that are associated with increasing sensory arousal thresholds. Brain waves recorded during wakefulness and REM are lacking in synchronicity with ocular movements in both states\textsuperscript{12-14}.

This basic physiology of sleep changes include greater preponderance of REM sleep in children, a peak in Stage 1 and 2 sleep in the age range 35-50 years and a marked decrease in slow wave sleep in the age range 20-25 years\textsuperscript{12-14}. There is a major gender difference in age-related alterations in sleep patterns, where more conservative changes occur in women\textsuperscript{13}.

While much interest has focused on centers of the brain that induce sleep, the suprachiasmatic nucleus (SCN) in the hypothalamus plays a pivotal role in sleep/wake
The SCN appears to be the regulator of times of both sleep and “wake” states. There are more structures in the brain that promote wakefulness compared with those that cause sleep.

Many “recuperative” factors occur during restful sleep. During sleep, muscle tissue is repaired, neuronal regeneration occurs in cerebral cortex and new synaptic connections form with memory registration. Sleeplessness is associated with reductions in core body temperature, impairments of immune function, increased variability in heart rate, reduction in growth hormone secretion, change in mood (depression), alteration in appetite (orexigenic status), diabetogenic tendencies, psychomotor retardation and other disorders.

The Impact of Insomnia

Insomnia causes a litany of sociobehavioral, economic, medical and even political problems. A strong association between sleeplessness and poor health (perceived or overt), chronic diseases, overutilization of medical services, industrial or work productivity and excessive use of medication, with associated iatrogenic disease. These associations exist with clarity in the medical literature.

I have described the consequences of insomnia under two broad categories. These categories are the “obtrusive” (overt) consequences or the “unobtrusive” (less obvious) consequences (Table 1).

Table 1. Consequences of Sleep Deprivation (A Summary)

<table>
<thead>
<tr>
<th>OBTRUSIVE</th>
<th>UNOBTRUSIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced quality of life</td>
<td>Stress drives</td>
</tr>
<tr>
<td>Poor daytime function</td>
<td>Poor coping mechanisms</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Interpersonal problems</td>
</tr>
<tr>
<td>Dozing</td>
<td>Errors, e.g. medical personnel</td>
</tr>
<tr>
<td>Poor concentration</td>
<td>Adverse drugs events</td>
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<tr>
<td>Hyper-irritability</td>
<td>Weight gain</td>
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<tr>
<td>Memory deficit</td>
<td>Promotion of Syndrome X</td>
</tr>
<tr>
<td>Lack of motivation</td>
<td>Immune impairment</td>
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<tr>
<td>----------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Hormonal dysfunction</td>
</tr>
<tr>
<td>Blues, depression</td>
<td>Premature Aging</td>
</tr>
<tr>
<td>Accidents</td>
<td>Digestive upset</td>
</tr>
<tr>
<td>Increased utilization of medical care</td>
<td>Premature death</td>
</tr>
<tr>
<td>Looking unkempt</td>
<td>Cancer risk increased</td>
</tr>
<tr>
<td>Decreased work performance</td>
<td>Poor blood sugar control in diabetes</td>
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</tbody>
</table>

It is useful to classify insomnia in terms of primary insomnia of unknown etiology and co-morbid insomnia (secondary insomnia)\(^3,16-18\). Secondary insomnia is often due to a combination of factors including: medical or psychiatric disease, adverse effects of medication, poor sleep hygiene, the presence of periodic limb movement or sensory disorders (Restless Legs Syndrome, RLS), cardiorespiratory disease (sleep apnea) and disorders of circadian rhythm\(^1,3,16-20\).

**Co-morbid Sleeplessness (Insomnia)**

The interaction of sociobehavioral, medical and psychiatric disturbance with insomnia is a very important, complex topic. Without a clear understanding of co-morbid insomnia, a correct management approach to insomnia cannot be defined in many patients. To define sleep hygiene as a co-morbid state is somewhat problematic, but poor life routines and adverse environmental factors are enemies of restful sleep\(^1\). Daytime idleness or excessive emotional or physical activity prior to sleep should be avoided\(^1,3\), with the exception of sexual union. Substance abuse (alcohol, sugar, smoking, illicit or certain prescription drug use) prior to bedtime play a variable role in the causation of poor sleep\(^1,21,22\). The bedroom should not be a “playground” or work area and its ambience should be agreeable. As simple as these latter issues appear, they are often overlooked as a cause of insomnia.

Many medical or psychiatric disorders are co-morbid factors in the insomnia\(^1,3,6\). Any disease causing chronic pain or cognitive decline interferes with sleep. Special
mention is required for menopause, chronic airways disease, obesity or urological disease. In many cases, the medications used to treat these disorders are the problem. Common drug causes of insomnia include: antidepressants, antihypertensives, sympathomimetics, cancer chemotherapy, certain hormonal drugs and others (caffeine, cough and cold preparations, opioids, etc)\textsuperscript{1,3}.

The individual with sleep apnea should undergo special management because of the multiple problems presented by this disorder\textsuperscript{1,3,23}. The individual with obstructive sleep apnea has a greater occurrence of hypertension, Syndrome X, gastroesophageal reflux disease (GERD), cardiovascular disease, stroke, obesity, daytime “narcoleptic” episodes and sudden death\textsuperscript{1,3,23}.

The body has its own inner biorhythms (circadian rhythms)\textsuperscript{16,24}. These rhythms are impacted by shift work and travel through time zones. A specific sleep disorder due to circadian rhythm is the “delayed-phase-sleep-syndrome.”\textsuperscript{3,25} In this syndrome there is failure to fall asleep associated with failure to awaken at “social” times in the morning. This condition is more common in teenagers whereas the advanced sleep phase syndrome can be encountered more often in elderly people\textsuperscript{3,25}. This disorder may be made worse by hypnotic drug treatments.

**Diagnosis of Sleep Disorders**

There are many disadvantages and limitations of current approaches to the major public health problems presented by insomnia. Several factors emerge in this situation including: lack of public awareness of the adverse consequences of sleeplessness, inappropriate or premature use of drugs for sleep (with minimization of their side effects), missed diagnoses of insomnia and a prevalence of medical ignorance about the science of sleep\textsuperscript{1,3}. A rational diagnostic approach for healthcare givers is summarized in Table 2.

- Public and professional education on sleep
- Vigilance for sleep problems
- Routine incorporation of a sleep history in clinical practice
- Structured questions asked about sleep
- Corroborative information from bed partners
- Care with medications that cause insomnia
- Detailed knowledge of sleep hygiene
- Identification of parasomnias
- Routine laboratory tests
- Identification of co-morbid factors
- The use of sleep diaries, where relevant
- Adequate follow up
- Lifestyle history

Table 2. Diagnostic approaches to sleep problems and initiatives

In cases of doubt, the healthcare giver should refer a patient to a specialist sleep center for evaluation\(^2^3\). Several indications have been proposed for the use of polysomnography or specialist referral\(^2^3\). These indications include: sleep apnea, overt behavioral problems related to sleep, severe daytime sleepiness, parasomnias, neurological deficits, recalcitrant insomnia and psychiatric or severe psychosocial disorders that are believed to be sleep related\(^3,2^3\). The cost-effectiveness of detailed sleep studies, performed in specialized sleep laboratories, remains arguable, especially when it is utilized in the management of mild to moderate sleep disorders.

Management/Therapeutics

The ideal management of sleep disorders involves a multipronged or multidisciplinary approach\(^1^\)\(^-^7\). The “sleep history” often uncovers many issues that require general or specific advice e.g. positive lifestyle change and detailed advice on sleep hygiene\(^1\). While it may be occasionally appropriate to prescribe a pharmaceutical for sleep early in the phase of treatment, premature use of hypnotic drugs should be avoided where possible\(^1\). A staged strategy using behavioral therapy, lifestyle change and nutritional support, with appropriate dietary supplements are the first-line management options of for mild to moderate sleep problems\(^1\).

Combination behavior therapy (CBT) for sleep disorders is grossly underutilized in medical practice\(^1,2^6\). Such underapplication of CBT is due to the potential complexity of this intervention over a prolonged period of time, in some people. That said,
techniques such as cognitive therapy, detail paid to sleep hygiene, control of wakeful stimuli, sleep restriction and simple positive lifestyle change can all result in rapid improvement and good clinical outcome in the majority of people with sleeplessness\textsuperscript{1,26-28}. The idea that only a “sleep specialist” can apply these interventions is absurd and it renders valuable medical intervention for sleeplessness “non-portable” in the community.

Cognitive behavioral therapy is best incorporated into the concepts of “mind-body” medicine, but it fails to pay enough attention to the “body-mind” linkages\textsuperscript{1,2,6}. Behavioral therapy recruits the ability of a care-giver to change an individuals approach to insomnia, belief systems about sleeplessness, control stimuli that promote wakefulness, stop people lying in bed awake and utilize relaxation responses\textsuperscript{1-7}. The value of this mind-body approach is related to the fact that most cases of primary insomnia are linked to psychological issues\textsuperscript{1-7,26,27}.

Sleeplessness may build a vicious cycle of failed sleep with consequences that provoke anxiety about sleep. This anxiety can mount to a level that interferes with the actions taken to promote sleep. The use of CBT in co-morbid insomnias, e.g. depression or malignant disease, may be quite valuable\textsuperscript{27,29}. It is estimated that four out of five people with persistent insomnia may benefit variably from CBT (mind-body) interventions\textsuperscript{3,27-29}.

Mind-body interventions can be expanded into simple “10 point” sleep naturally plans (Table 3)\textsuperscript{1}.

1. Assess your sleep duration and quality. Make a sleep journal and ask your sleeping partner about your sleep habits.
2. Regularity in sleeping and waking patterns is important to set the stage for regular sleep cycles. Attempts to awaken and go to bed at similar times everyday are beneficial. Regimentation of sleep is a valuable activity.
3. An individual who cannot sleep should not spend a long time lying in bed, tossing and turning. On occasion, one may be best advised to engage in activity.
4. Daytime “napping” is an arch-enemy of restful nocturnal sleep, especially in the elderly.
5. Individuals should avoid dietary substances containing stimulants, such as caffeine and alcohol at night. Smokers should abstain; nicotine acts as an energizer.

6. Meditation and relaxation with some time to examine the events of the day is valuable in many insomniacs.

7. A bed is for sleep (and sex), not for work, worrying or eating.

8. Pay good attention to the bedroom environment. Encourage partners to get help with snoring. Otherwise, partners can be encouraged to sleep elsewhere, although this may not be popular advice! Do not ignore Sleep Apnea.

9. If eating is planned in the two hours preceding bedtime, then food choices must be appropriate, e.g. milk and light, healthy snacks.

10. Regular exercise helps sleep – but late-night exercising must be abandoned, as the endorphins produced from exercising serve to keep the body energized. Healthy sex promoted restful sleep.

Table 3. The author’s 10-point Sleep Naturally Plan (Holt S, Sleep Naturally, Wellness Publishing, Little Falls, NJ, 2003).

Pharmaceuticals for Sleep

There are many chemical messengers in the brain that promote sleep or wakefulness. Altering the action of these messengers, most notably using gamma-aminobutyric acid (GABA) blockers, has guided pharmaceutical research on hypnotic drugs. While the brain takes the lead in sleep/wake states, sleep is a highly complex cascade of physiological events in the body. Many of these events occur outside the central nervous system, e.g. changes in immune function or gastrointestinal physiology. The pharmacological control of sleep exemplifies the problem with single (or focused) drug-receptor effects on complex body functions such as sleep.

Restoration of the harmony of the entire body is a desired approach to promote healthy sleep compared with a pharmaceutical approach that involves single, drug receptor actions. I see drug use in sleep disorders the “reductionist” circumstance of modern allopathic therapeutics. While pharmacological research has many putative targets for receptor agonist or antagonist actions (neurotransmitters or modulators) to
approach in sleep correction, the current focus of activity rests with benzodiazepine-receptor or melatonin-receptor agonists\(^3,6,30-35\).

Previously popular benzodiazepine drugs used for sleep induction, included diazepam and flurazepam, both of which may not be a therapeutic match for the herb Valerian (a natural benzodiazepine agonist)\(^1,36,37\). The pharmacotherapeutic trend in modern pharmaceutical research has been to seek compounds with shorter blood half-lives. The half-life of modern benzodiazepine drugs has been reduced from up to a couple of days (flurazepam Dalmane\(^©\)) to a couple or few hours, or so (eszopiclone, Lunesta\(^®\) and zolpidem AmbienCR\(^®\))\(^31\). The presence of enhanced receptor actions of modern hypnotic drugs is sometimes arguable.

The drug zolpidem (AmbienCR\(^®\)) has to be given in sustained-release form to achieve reasonable total sleep times\(^3\). While pharmaceutical companies argue that this approach with controlled-release formulations enhances sleep time with “limited,” residual, daytime effects, these proposals may be questioned. In some circumstances, controlled-release, pharmaceutical formulations are notoriously unreliable and it may be that the delayed absorption of zolpidem may result in “hangover” or mental impairment in some circumstances. The performance of pharmaceutical formulations is impacted by many factors, such as co-existing disease, dietary factors and gastrointestinal disturbance. Many of these factors that alter drug absorption and disposition are present in the insomniac\(^1,3\).

A powerful group of influences have served to minimize or frankly ignore the troublesome or life-threatening adverse effects of sleep drugs. These drugs comprise a multi-billion dollar global market. Protectionism of such markets is understandable. All prescription or over-the-counter (OTC) drugs, used as hypnotics, possess disadvantages. All may cause prolonged drowsiness or retarded psychomotor function\(^1,6\). Many cause gastrointestinal upset, dizziness, light-headedness or headache\(^6\). Many are expensive and all can cause tolerance with the development of variable degrees of dependence\(^1,6\).

I believe that OTC sleeping drugs are quite dangerous in the elderly. Many of these drugs are antihistamines that are used because of the side effects of drowsiness that are experienced with these drugs\(^1\). Anti-histamines are present in dedicated OTC
sleeping tablets and in many cough and cold remedies\(^1\). Anti-histamines have long half-lives and produce exceptional and protracted hangover or drowsiness in a significant number of users, especially the elderly. Overall, these OTC drugs possess anti-cholinergic effects, resulting in the common occurrence of blurred vision, dry mouth and dry mucus membranes. Less common, but very serious side effects of anti-histamine drugs, include: aggravation of urinary symptoms in individuals with prostatic enlargement, episodic disorientation in the elderly and the potential precipitation of cardiac arrhythmia. I believe that prescription and OTC hypnotic drugs are responsible for increasing the risks of injuries or “falls in the night,” in certain elderly people. An elderly person taking a long-acting or potent sedative drug may be more likely to rise from their bed in the night for urination and fall, with resulting bone fractures. I believe that the combination of osteoporosis in the elderly with uncontrolled use of hypnotic drugs is a very serious risk circumstance. The magnitude of the adverse effects of OTC hypnotic drugs remains unknown because such effects require voluntary reporting. Such reporting is often incomplete.

An unresolved controversy concerning hypnotic drugs is an alleged association between their use and premature death or increased mortality. The pivotal research in this area is reported by D.F. Kripke et al in two studies\(^3\). In the 1959, ACS (American Cancer Society) sample, 50% more individuals who frequently used sleep drugs died compared with those who did not take these drugs, matched for age, sex and health status\(^3\). In the 1982, ACS sample a similar outcome was noted, but in this latter sample individuals were carefully matched for age, sex, race, education and thirty two health risk factors\(^3\). The individuals who had taken hypnotic drugs in a dosage of 30 tablets or more per month had a 25% greater mortality than those who did not take these medications\(^3\). In addition, up to a 15% increase in mortality was recorded as a consequence of infrequent use of sleep drugs\(^3\). Kripke et al concluded that taking thirty or more sleeping pills per month produced a risk of death that was approximately equivalent to smoking one package of cigarettes per day\(^3\). While argument prevails about the conclusions that hypnotic drugs account for excess mortality, the overall risks
of the long term use of hypnotic drugs remains underexplored. (www.darksideofsleepingpills.com)\textsuperscript{38}.

Modern hypnotic drugs may cause eating disorders, aggravate some parasomnias, induce somnambulism and impair a person’s ability to drive or operate machinery\textsuperscript{3,30-35,38}. The safety of the long term use of drugs for sleep is not clear and they are to be avoided in pregnancy and childhood. While other compelling reasons exist to avoid hypnotic drugs, simple, safe, viable alternatives are required. These viable alternatives involve the use of mind-body medicine and natural, nutritional support of sleep with effective dietary supplements\textsuperscript{1}.

**Nutritional, Botanical and Herbal Support for Sleep**

A large body of folklore, ethnobotanical and scientific literature supports the use of nutrients and plants or their extracts in sleep promotion\textsuperscript{1,36,37,39}. Botanicals or nutrients that can be used with melatonin to assist in promoting restful sleep are listed in Table 4.

<table>
<thead>
<tr>
<th>Herbs</th>
<th>Valerian, Chamomile, Ashwagandha, Passionflower, Lemon Balm, Catnip, Skullcap, Hops</th>
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</thead>
<tbody>
<tr>
<td>Hormones</td>
<td>Melatonin</td>
</tr>
<tr>
<td>Nutrients</td>
<td>Amino acids, 5-HTP, Magnesium, Niacin (B3), Peridoxine (B6), Folic Acid</td>
</tr>
</tbody>
</table>

**Table 4. Synergistic Supplements for Cascades of Sleep**

Melatonin has received most use as an adjunct to sleep and it plays a special role in reversing jet lag or altered circadian rhythms in shift workers\textsuperscript{40}. Melatonin is only secreted in significant amounts at night leading to its description as “the vampire hormone.” Exposure to light suppresses melatonin secretion abruptly and its secretion
declines with age. Controlled studies show that melatonin administration shortens sleep induction time and reduces the impact of nocturnal stimuli to arousal, but it may not consistently increase total sleep time\textsuperscript{40}. While melatonin has many variable actions, e.g. antioxidant or anti-cancer effects\textsuperscript{41}, it causes tolerance, requiring increased dosages over time for sleep assistance\textsuperscript{6}. I do not recommend melatonin alone for sleep because it has questionable safety at high dosages (greater than 4mg per day)\textsuperscript{6}.

While many nutrients, micronutrients or nutritional co-factors may enhance sleep, those of maximum use in supplement form are magnesium, calcium, selected amino acids and anti-stress vitamins of the B complex (Table 4)\textsuperscript{1,6}.

Several botanicals or herbs in whole or extracted forms support sleep or exert stress-busting, anxiolytic effects (Table 5)\textsuperscript{1,6}.

<table>
<thead>
<tr>
<th>HERB/BOTANICAL</th>
<th>COMMENT</th>
</tr>
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<tbody>
<tr>
<td>Valerian</td>
<td>Sedative, anti-myoclonus, GABA breakdown inhibition, carminative no hangover of benzodiazepines, adaptogenic</td>
</tr>
<tr>
<td>Chamomile</td>
<td>Calming, analgesic, anti-inflammatory, antioxidant, carminative</td>
</tr>
<tr>
<td>Ashwagandha</td>
<td>Nervine, adaptogenic, mild sedative, “Indian Ginseng”</td>
</tr>
<tr>
<td>Passionflower</td>
<td>Nerve tranquilizer</td>
</tr>
<tr>
<td>Lemon Balm</td>
<td>Sedative, anti-spasmodic, nerve, value in depression, GI soothing</td>
</tr>
<tr>
<td>Catnip</td>
<td>Mild sedative, anti-anxiety</td>
</tr>
<tr>
<td>Skullcap</td>
<td>Anti-anxiety without drowsiness, adaptogenic</td>
</tr>
<tr>
<td>Hops</td>
<td>Sedative-hypnotic, smooth muscle relaxation, close cousin of marijuana</td>
</tr>
</tbody>
</table>

Table 5. Herbs and botanicals for sleep. These herbs can be used with nutrients and melatonin in effective dietary supplements to support the body function of sleep.
A Natural Sleep Protocol: The Sleep Naturally Plan

With clarity, my suggestions for the management of many people with insomnia are somewhat contrary to conventional medical practice. My dissonance is based upon clear evidence that there is overuse of pharmaceuticals for the correction of sleep disorders. The best model of care for insomnia of diverse course may be the interventions that I propose, which are consistent with the practice of Integrative Medicine. I would welcome suggestions that may improve the Integrative Medicine model, which I do not believe is experiencing benefit from drug overusage. If sleeplessness cannot be corrected by positive lifestyle change and behavioral therapy or mind-body medicine, I propose nutritional support with herbs, nutrients and melatonin, as a first line option. Experts in therapeutics may argue that this approach has not been subject to controlled clinical trials, but the synergistic combination of natural ingredients that I have proposed have been used in millions of unit dosages in dietary supplement format without any reports of significant adverse effects and a high level of consumer satisfaction.

The reason for the emerging epidemic of sleeplessness is not clear, but it seems to be a global phenomenon. The solution to this epidemic is more rooted in correction of adverse lifestyle than it is in any promise of a new pharmaceutical. My dissonance is justified by taking hypnotic drugs as one example of the pernicious “overmedication” of American citizens. Americans are the greatest users of pharmaceuticals in the world, per capita, but general health and wellbeing ranking shows that Americans fall into the 40th to 50th position compared with other countries. Something is clearly wrong with this situation and the overuse of prescription or OTC hypnotic drugs may be one of many examples of the increasing public health concern about drug overutilization. I make no apologies for my questioning of standard allopathic approaches to insomnia.
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