Abstract

Ubiquinone is one of the two most important essential nutrients (the other being ascorbic acid). These two molecules, along with other essential nutrients, have been rejected as unpattentable and unprofitable by certain “authorities” and interests, according to exposés by Pauling and others. This has been one of the most lethal errors of modern medicine because no cell, organ, function or remedy can avoid failure unless essential nutrients, especially these two, are optimal. Supplementation of both is mandatory: for ascorbate, lifelong (since humans can’t synthesize it); for ubiquinone, increasingly with age. In this update, to facilitate study of ubiquinone, we seek to assemble in one place vital information that is not widely known.

Introduction

Ubiquinone has been listed for years as an essential nutrient in the Physicians’ Desk Reference (PDR). The chemistry, history, and the many clinical trials that established the safety and efficacy of ubiquinone were well described in 1995 by one of the leaders in this work, Peter H. Langsjoen, M.D., FACC, in his Introduction to Coenzyme Q10. In the 1997 PDR, Langsjoen’s “Intro” is cited but the full text is not in print. With his permission, we placed the entire “Intro” on a web site with much other material in 1996. From his 65 references, we transferred selected reports to the bibliography here and numbered them as follows: nine large scale placebo controlled clinical trials; nine additional open-label trials, including the 2,664 patient multicenter study in Italy reported by Baggio, and the Proceedings of eight international symposia. The web site created in 1996 as a “Physicians’ Update on Coenzyme Q10”, was made in response to the request from Clinical Chemistry that we determine the demand for blood tests. Clinical Chemistry would need to robot (automate) the complex 14-step HPLC assay (provided to Ely by Karl Folkers) sufficiently to make it efficient to run and affordable. To determine if the demand for the ubiquinone blood test justifies this considerable effort, the web site asks that physicians complete the extremely brief electronic questionnaire linked to the site.

Ubiquinone Turnover

Naturally, many details concerning the pharmacokinetics and clinical use of ubiquinone have been learned since the 1970s in the cited clinical trials, symposia and in related research. Possibly the most important details are those related to ubiquinone body pool and turnover rate that mandate human supplementation. Adult human body pool has been found to be approximately 2 g and requires replacement of about 0.5 g/day based on its average turnover rate of about 4 days in various tissues. This must be supplied either by endogenous synthesis or from exogenous sources. Synthesis decreases progressively in humans above age 21. Furthermore, the average ubiquinone content of the western diet is less than 5 mg/day. Thus, ubiquinone supplementation appears to be the only way for older people, and certainly the ill, to obtain the major proportion of the 0.5 g/day need. Failure to supplement by the aged, ill or stressed, can have tragic consequences in the form of irreversible damage in the brain, other organs and mitochondria everywhere. In addition to production of adenosine triphosphate (ATP, molecules for energy), and maintenance of cellular and mitochondrial membrane fluidity, ubiquinone has a possibly even greater value. This is its free radical quenching
ability (50 times greater than vitamin E), that prevents the above mentioned irreversible oxidative damage.

In Professor Littarru’s authoritative 91-page book, he devotes 65 pages (71%) to ubiquinone’s defense against free radical damage. He points out that knowledge of mitochondrial aging in unsupplemented mammals has been published since 1985. Regarding the aging mechanism, Littarru and others have stated that low values of ubiquinone permit oxidative damage to the DNA of mitochondria, permanently impairing their ability to function. If, by supplementation, the ubiquinone level is restored to its proper value, the rate of oxidative damage will be lessened, but the impairment remains. Doesn’t it appear that physicians who tell their patients not to take ubiquinone, are saying: “Age more rapidly, have more health problems including cardiopathy, intellectual impairment (especially strokes) and die early”? Isn’t this what is happening in America today?

Safety of Ubiquinone

In many large-scale clinical trials, oral ubiquinone has been shown to be safe and efficacious at blood levels of about 4 ppm (considered pharmacologic and attained by 800 mg/day). In addition, even at levels of 80 ppm measured by the Japanese in 1984 with an IV ubiquinone preparation, only beneficial effects were reported. A new injectable liposomal ubiquinone is available from Eisai. A caveat: in patients with alcalinized stomachs, oral Candida can colonize upper gut (potentially lethal); before prescribing ubiquinone, their physicians should study Marshall et al. Our studies show that ubiquinone enhances growth of Candida albicans.

Stroke

Since 1972, in studies of stroke in three animal models (dog, rat, gerbil) ubiquinone was the only agent giving complete protection and this was over two times more often than the next best agent (naloxone) of the many tested to date. Some of the animals were pretreated and some post-stroke (less than 12 hrs). None of the 50+ synthetic stroke agents tested in humans has yet proven successful as of February 2000. If mainstream medicine has any humanistic motivation, why doesn’t it use ubiquinone in the interim?

The first human observation using ubiquinone was in a patient predicted by the very experienced stroke specialists in a large California facility to remain permanently comatose. She recovered completely after about 10 days in coma. She had been in treatment for a memory problem with oral ubiquinone 400 mg/day for a month prior to an accidental head trauma with massive hemorrhage. In a second case (unpublished), a woman in her sixties, the mother of Dr Fudenberg’s former secretary, had a similar stroke with the same prognosis of permanently vegetative; he traveled from South Carolina to Oklahoma, got the patient out of hospital and gave her 400 mg ubiquinone b.i.d. (starting four days post-stroke, which we felt would be too late) and she recovered to much better than her pre-stroke condition (i.e., mental acuity, speech, agility, equal to what she had experienced in her 40s). There has been a third case which we do not “advertise” because it is extremely important to elevate ubiquinone as rapidly as possible to minimize the ischemic reperfusion injury. This is a 70-year old male professional dancer in Seattle who was given ubiquinone in similar oral dosing starting on the eleventh day and made progress much above predicted; he regained speech and ability to do dance steps but had difficulty with names and his recovery plateaued after a few weeks; his stroke was not comatose and his recovery was not complete to his pre-stroke condition. Can’t the medical (and lay) readers of this journal help stimulate a grass-roots evaluation of this simple innocuous treatment? We emphasize that we are not ad-
vising people to self-treat. However, every-
one must realize that, each year in the
U.S.A. alone, over 650,000 families have a
loved one hospitalized for stroke. Only 1/4
of these escape death or permanent disabil-
ity. The families have a right to know that
ubiquinone exists at their health food
stores, has the properties described above
and appears likely to avert the tragic prog-
noses. If you readers pass this information
to such families, many, in their desperation,
may elect ubiquinone. We request the read-
ers suggest: (1) this be done with the best
open-minded preventive medicine supervi-
sion available; and (2) the supervising phy-
sician report by email (apresi@aol.com) the
patient identification, date of stroke, treat-
ing stroke center, prognosis, time delay
before ubiquinone (swallowed or intuba-
tion), dosage including other agents, and
progress up to four weeks post-stroke.

Ubiquinone in Cardiology

**Negative “Studies”:** A very few nega-
tive studies from the early 1990s up to
present have reported lack of beneficial
effects of ubiquinone for congestive heart
failure (CHF). Fundamentally, these nega-
tive studies have been criticized as cases
of too little ubiquinone, for too short a time
and too late in the course of CHF in the
trial patients. Correct treatment should in-
clude the essential nutrients (ubiquinone,
vitamin E, and ascorbic acid) and no
statins. Self-appointed “experts” who have
no experience in treating CHF correctly
have praised these few negative “studies”
while ignoring the vastly greater literature
cited above including the large scale trials
demonstrating the positive aspects of ubi-
quione. Could the negative studies have
been “designed” to produce failures? Is this
action designed to oppose acceptance of
the low cost (unprofitable), non-toxic (en-
dogenous), versatile ubiquinone modality?
Certainly the investigators and extollers of
these negative “trials” appear to be totally
oblivious of the fundamental physiology of
ubiquinone requiring its constant replace-
ment at 500 mg/day by synthesis from ex-
ogenous substrate or by supplementation.

**Positive Studies:** Clinical observations
of cardiologists who have had extensive ex-
perience with the use of ubiquinone (such
as Peter Langsjoen) find dramatic improve-
ments in heart function in CHF patients
treated with ubiquinone prior to the devel-
opment of irreversible damage. While the
optimal dose of ubiquinone in the treat-
ment of congestive heart failure is not es-
tablished, it has become clear over the past
15 years, that 100 mg per day (the dose used
in some of the negative studies) is subopti-
mal for the majority of patients. A higher
dose of ubiquinone for a longer period of
time has demonstrated highly significant
benefit in many previously published tri-
als. An extensive review of ubiquinone use
for cardiovascular disease (CVD) in 34 con-
trolled clinical trials and several open-la-
bel and long-term studies has recently been
published.42

**Statins: Toxic Misuse:** Karl Folkers,
the frequently honored chemist who first
determined the structure of ubiquinone
in 1958 and was Director of Research for
Merck for 20 years, warned in 199043 that
heart disease is caused or worsened by
the depression of ubiquinone that is as-
sociated with statin use and that ubi-
quione must be supplemented ade-
quately in patients given statins. Oth-
ers have also documented this high level
mandate for use of ubiquinone with
statins.32,42 Theoretically curable CVD
patients on statins will progressively de-
compensate and decrease ejection frac-
tion if given only 100mg ubiquinone/day
or less. They can reverse these losses and
recover if given sufficiently greater than
200mg ubiquinone/day. If the lethal ef-
effects of violating this higher need for ubi-
quione created by statins are over-
looked, CVD patients are trapped in an
expensive downward spiral to death and
vastly more dollars are spent on their care
than if given adequate ubiquinone. Ironically, statins may only be needed in the truly rare familial hypercholesterolemias. It is well known that: (1) cholesterol is not a risk factor for CVD unless LDL is oxidized; and (2) this is simply prevented by supplementation of vitamin E in nearly all humans.\(^{44,45}\)

Ubiquinone and Ascorbic Acid (AA)

There can be little expectation for significant improvement in ejection fraction or any other parameter of cardiovascular function without high AA levels. These levels are necessary for hydroxylation reactions in the constant restoration of the structural proteins, collagen and elastin.\(^{46}\) Virtually all unstressed mammals need roughly 50 mg AA/kg body weight daily, or \(\sim 3.5 \text{ g/70kg}\) in humans. Of course, CVD patients may not be exactly “unstressed”. If AA intake is only 60 mg or 200 mg (the current and proposed RDAs for AA), patients would likely not have frank clinical scurvy. However, at these low intakes, it is extremely unlikely that they could restore or maintain youthful elasticity of blood vessels to increase ejection fraction, even though ubiquinone is supplied. Moreover, glycemic level must be controlled; AA cannot enter cells of hyperglycemic tissues because glucose competitively inhibits its insulin-mediated active transport (Ely, 1972, unpublished). Thus, modest hyperglycemia can cause scorbatic conditions to exist in the intimal surface of blood vessels even when plasma AA levels are reasonable.

Glycation and Aging

Ely discovered in animal model work (and confirmed with Warner et al in a study of 300 human patients) that elevated plasma AA levels antagonize glycation of hemoglobin and all other proteins, which improves health and slows aging.\(^{47}\) Unfortunately, we are then faced with the nuisance that glycated hemoglobin reads falsely low when used as a measure of average blood glucose level for purposes of glycemic control. Bliznakov demonstrated restoration of youthful thymic response against viruses and tumors and major increases in lifespan of very old mice given ubiquinone.\(^{48}\) There is ample evidence that high levels of ubiquinone, and AA, slow the detrimental biochemical, structural and other changes that occur with aging in all mammals. Ubiquinone may reverse some age-related bioenergetic degradation that acutely affects the systems with the highest energy demand (cardiovascular and immune). Failure in these systems is a major cause of morbidity and mortality in the elderly. However, it has been known since 1985 that mitochondrial aging (in all systems) that accumulates in intervals when ubiquinone is low, especially the brain, is not reversible. Supplementation of ubiquinone and AA with glycemic control should be considered by all adults, especially the elderly, ill and stressed. Amounts of AA needed in health and disease have been discussed previously.\(^{5}\)

Acknowledgements

Support from Applied Research Institute and the assistance of H. F. Krone are gratefully acknowledged.

References

7. Kamikawa T, Kobayashi A, Yamashita T, Hayashi...
A Brief Update on Ubiquinone (Coenzyme Q₁₀)


