# Hypochlorhydria and Multiple Organ Failure: A Leading Cause of Death in the Intensive Care Unit

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*Abstract*

*Various kinds of multiple organ failure (MOF) are briefly compared. We argue that many MOF's result from those esophageal perforations due to oral Candida. We focus on a "silent" MOF associated with gastric hypochlorhydria and describe a prophylactic regimen that: (1) greatly reduces oral Candida and is predicted to stop their esophageal perforations; and (2) prevents Candidal colonization in the small intestine. The regimen uses: cetylpyridinium chloride (CPC) to decimate the oro-pharyngeal source of Candida; a slow release caprylic acid administered orally by intubation (or capsules) that antagonizes Candida colonization of the small intestine; and biotin to prevent conversion of Candida to the invasive hyphal form. We anticipate early use of the regimen should prevent all of the sequelae that result from esophageal perforation and from colonization of the duodenum and jejunum in patients and in non-patients who are using otc proton pump inhibitors ad lib to depress gastric acidity.*

*Abbreviations: BSAC = British Society of Antimicrobial Chemotherapy; CanDPJ = Candida colonization of the duodenum and proximal jejunum; CMI = Cell Mediated Immunity; cvd = cardiovascular disease; CPC = cetylpyridinium chloride; Fn = Foundation; M&M = morbidity & mortality; otc = over the counter; PPI = proton pump inhibitors; Q10 = coenzyme Q10 (ubiquinone)*

## Introduction

Multiple Organ Failure (MOF) is a MESH term defined in 1983 as a progressive condition usually characterized by bacteremia and sepsis-induced combined failure of several organs such as the liver, lungs, kidney, pancreas, along with some clotting mechanisms, often postinjury or postoperative. This type of "lethal crisis" MOF is in stark contrast to the one of interest here, a "silent" lethal MOF, undetected by patient or staff until too late. Many etiologies have been reported for MOF. Leading authorities in surgery have called MOF "the major challenge to patient survival."[1] In spite of rapid growth in overwhelming complexity during the past two decades, many features of MOF have been catalogued via these surgeons' heroic efforts to save lives. Significant advances in MOF prevention have been made by Maier. His work over the past 20 years has culminated in a trial that is discussed below (see Optimizing Antioxidants in Treating Infections). Annual US toll from all types of infections is: nearly 200,000 premature deaths (over 2 million years of life lost before age 65), over 42 million hospital days, costing over $17 billion.[2] Overall U.S. health care cost including both private and public funds exceeds $1 Trillion (i.e. over one sixth of the national debt) or $4,000 per capita.[3]

Between 1979 and 2000, rate of sepsis due to fungal organisms increased over 200 percent. Sepsis and septic shock continue to be major causes of morbidity and mortality in the United States, matching even the mortality from myocardial infarction. The increase in fungal infections during the past two decades has been attributed to the increased use of immunosuppressive and antineoplastic agents, prosthetic devices and grafts, broad-spectrum antibiotics and hyperalimentation.[4] Patients colonized with Candida show severe organ

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dysfunction.[5,6] Isolation of Candida spp. within the first week after surgery has been associated with extreme mortality (55%).[7] In addition, high risk colonized patients may not always demonstrate perioperative fungemia.[8] A highly specific and sensitive routine test for the diagnosis of Candida infections does not exist and clinical signs of fungal infections are rather unspecific.[4] Thus, although fatal esophageal perforation was reported long ago in 1835 (see Hyphal Forms of Candida), candidiasis has continued to grow. It has become possibly the commonest, most involved, and most often lethal, infectious complication dominating M&M and care cost in numerous diseases and patient classes. In many conditions including AIDS, burns, cancer, critically ill, drug addiction, dyspepsia, MOF, surgical sepsis, and various cognitive disorders, Candida is a causative or coexistent factor. Growing evidence suggests it may be a more common cause of death than the primary conditions, especially when colonizing the duodenum and proximal jejunum (a condition we call CanDPJ). Marshall et al. did much early and important work (including development of an objective scoring system) on the microbiology of MOF[5,6] listing Candida as most prominent in organ failure, but did not explore the role of hypochlorhydria re oral Candida. We discuss herein several previously unknown or unappreciated factors that contribute to the increasing incidence of fatal fungal infections and MOF due to oro-pharyngeal Candida traversing the hypochlorhydric stomach to produce CanDPJ.

**On Diverse Types of Fatal MOF**

*Silent MOF.* The principal purpose of this urgent paper will be to: (1) provide a detailed introduction to the "silent" MOF caused by the dimorphic *Candida albicans* highly sensitive to gastric hypochlorhydria, an increasingly common condition in recent years (see below Hyphal Forms of Candida and Gastric Acidity: Life or Death); (2) describe a proposed prophylactic protocol (see below and Oral Q10 and CanDPJ Revisited); and (3) touch on the already understood extremely different sepsis-induced MOF and the esophageal perforation MOF that both have no special involvement with chlorhydria. Now we summarize first, the type MOF of most interest here. This first (ie, strictly fungal) "silent" MOF is caused only by the dimorphic *Candida albicans,* gives no warning and "precedes" septicemia which it usually "prevents" by killing the human host. "Silent" fungal MOF proceeds from the occult hypochlorhydric gastric reservoir directly into adjacent organs (see CanDPJ and Fungal MOF ) such as liver and pancreas without using the circulation. This fungal MOF is preventable if the hypochlorhydral host is aware or, preferably, if a supervising informed physician is aware of the prophylactic modalities described below. To our knowledge, treatment is rarely possible. Only prophylaxis is simply feasible and must be maintained as long as the host is hypochlorhydric.

*The prophylactic protocol* is designed: (1) to strongly minimize the oro-pharyngeal population of *C. albicans* (essentially eliminating it as a source of Candida for the upper GI tract): and (2) to render the duodenum and proximal jejunum (DPJ) continuously unsurvivable to Candida. It employs long-known, widely used, well tolerated, inexpensive, otc pharmaceuticals. The preventive modalities include: (1) the use of antifungal mouth rinses (containing cetylpyridinium chloride) to reduce oral fungi (see Regimen Components); (2) dosing with time-release caprylic acid (Mycopryl 680" capsules or powder, T.E. Neesby, Inc. Fresno, CA 93720) to minimize Candida survival in the DPJ; and (3) use of biotin supplementation to prevent conversion of Candida to the invasive hyphal form.

**Some Other MOF's**

Now, in sharp contrast to the essentially "silent" undetectable fungal MOF discussed above, we briefly comment on other types:

(1) The "lethal-crisis" MOF, involving explosive infection of organs, follows and is driven by septicemia. Its treatment usually includes, inter alia, appropriate intravenous antibiotics and modalities that address the derangement of the immune inflammatory response seen in this type of MOF.

(2) MOF that can occur in any organs after esophageal perforation can only be prevented by elimination of dimorphic Candida-like fungi from the oro-pharyngeal flora. This requires a CPC-Mycopryl (or equivalent) regimen.

(3) Esophageal perforation by dimorphic forms from oro-pharyngeal flora is a lesion that can result in a vast variety of disorders, most with high mortality. These usually require difficult uncertain treatment including aggressive surgical debridement and antifungal therapy (as empirical minima). It should be suspected that any ICU patient with oro-pharyngeal fungal flora may have any of these disorders, including incipient "silent" MOF rapidly progressing. Possible need for appropriate polyene or imidazole therapy should be considered immediately on admission. The outcome of monilial esophagitis can range in complexity from a treatable stenosis to an uncontainable candida mediastinitis; or, even worse, a rapidly changing combination that defies diagnosis.

### The Complex Relationship of Candida with Coenzyme Q10

Typical of the complications that accompany Candida, is the paradox we consider here that coenzyme Q10 (Q10) (ubiquinone), the safest and least toxic endogenous molecule (ie, far less toxic than water) can precipitate a lethal crisis if used naively. Supplemental Q10 has been documented to be an effective biological response modifier in most human diseases and in animal models of aging and stroke. In well-controlled studies Q10 has been shown to be safe and efficacious with no sign of toxicity at the highest blood levels achievable by oral or IV dosing. However, in a small fraction of patients, use of oral Q10 supplementation fails to elevate blood Q10. For example, in patients with CanDPJ symptoms, a large intake of Q10 may cause negligible rise in blood level, no clinical improvement (metabolic functions of CMI require Q10 for the ATP) and rapid progression to fungal MOF (due to Q10-stimulated expansion of Candida population[9]) and death (due to Q10 loss to the yeast). The author (Ely, unpublished) had hypothesized that CanDPJ might cause such an effect.

### Gastric Acidity: Life or Death

An intact stomach acid system has always been the principal defense against CanDPJ (as well as to *H. Pylori,* etc). In the modern era, a combination of time pressures and oral hygiene habits (or lack thereof) result in a very large fraction of the healthy population culturing an oral flora rich in Candida (etc.) fungal sp. throughout each work-day. In addition, hypochlorhydria is: (1) induced by stress and acute adrenal insufficiency; (2) more common in the elderly (the most rapidly growing segment of our populations); (3) more prevalent in the ill (who are so numerous in the US where average "quality of individual health" ranks 72nd (!) although dollars spent per capita ranks first (!) among the 191 UN member nations[10]); and (4) induced by the rapidly growing numbers who now are able to ignorantly self-treat with alkalinizing agents (proton pump inhibitors (PPI)) recently made available over-the-counter (otc); etc. Several other common modalities (vagotomy, antacids, etc.) compromise this barrier to CanDPJ and occur in a number of patient classes. In one study, Candida were found in gastric aspirate in 5% of patients (3 of 61) prior to vagotomy and in 62% (31 of 50) after.[11] CanDPJ has been reported to occur as little as four weeks after initiation of cimetidine therapy.[12] Goenka et al[13] found that regardless of the type of PPI used, acid-

reducing therapy is associated with increased severe fungal overgrowth in duodenal ulcer patients. Because of the existence of the above conditions at this time, it is expected that the incidence of MOF, one of the most incurable and lethal diseases, must be rising rapidly. It is urged that on autopsies of MOF deaths, the question be examined whether Candida is present, likely causal, and possibly the sole cause.

**The Origin of CanDPJ**

In 1953, Brown et al. reported in JAMA[14] that candidiasis had seldom been mortal in the many years past. However, the authors noted and emphasized the marked increase in the frequency of generalized and fatal fungal infections, especially by *C. albicans,* since the introduction and increased use of broad-spectrum antibiotics after World War II. Their paper case-reported five such deaths, all following broad-spectrum antibiotic therapy. Two of these were in dentists, aged 47 and 50, without serious illness (nb, Hg increases susceptibility via enzyme inhibition!). The authors cited a recommendation by the AMA Council on Pharmacy and Chemistry that a warning regarding the danger of moniliasis be added to the labels of certain broad spectrum antibiotics. Recent observations by the present author found no evidence of concern regarding this problem among clinicians in two large institutions, one medical center and one HMO. However, among "candida-conscious" investigators, there is a saying that "you cannot cure Candida until you remove Hg (i.e., amalgams)".

The 1950's AMA recommendation to warn of the increasing M&M of moniliasis due to antibiotics was not adopted despite its extremely low cost. More recently, a tentative four arm trial was suggested by the British Society of Antimicrobial Chemotherapy in 1994;[15] it was not adopted because of lack of sufficient data to justify its considerable cost.[16] Thus, most mainstream clinicians have no guidance for management of this involved problem. Clearly, it appears that the majority of patients who receive recurrent therapy with broad-spectrum antibiotics and experience the unavoidable derangement of gut flora, eventually restore normal flora. This occurs in large part because they are free of risk factors that tend to perpetuate escape of Candida from its tolerated status as an "innocuous commensal." However, unless their features are known, it is not possible to identify, report, and estimate the toll in M&M and costs of patient classes who constitute the minority who do not restore homeostasis. To this end, we identify certain presently unrecognized risk groups herein. As shown below, some of these risk groups are quite large in numbers (eg, the elderly), and all have incurred large costs. We seek to clarify some of the difficult problems and, most importantly, to propose rapid evaluation of possible prophylactic and therapeutic solutions.

CanDPJ which was almost never identified in spite of high morbidity (ca 50%), is actually becoming increasingly recognized today. This form is observed to arise rapidly in patients in medical centers of metropolitan as well as developing nations. It occurs most often in surgical patients, especially in ICU, and is usually attributed to nosocomial factors (antibiotics, catheters, etc.). In addition, however, some other factors exist in many patient groups, some quite large, producing clinical emergencies because these factors are still not recognized. These include: (1) inadequate production by the ill patient of endogenous Q10 and failure to administer exogenous Q10 (whose very existence and functions are entirely unknown to many physicians); (2) low body ascorbate pool (<1 gram is almost universal in stressed patients): the pentose pathway (providing ribose necessary for CMI mitosis and phagocytosis) runs at a rate proportional to intracellular ascorbate; Maier reports remarkable success in hopeless surgical patients with in-

travenous ascorbate[17]; (3) candidiasis is either unsuspected or regarded as a minor secondary condition; (4) any other diseases mistakenly reported as intractable and severe when these conditions were due to unrecognized coincident candidiasis; and (5) Candida toxins' ability to produce symptoms of almost every known disease.[18]

The value of Q10 as an effective adjuvant has been reported in many human diseases, with marked dose dependent enhancement.[19] Its successful use in a steadily growing list that includes cvd, cancer, AIDS, Parkinson's Disease, aging, etc, in humans and animals has been reported.[19-33] The potential value of Q10 in cardiology was first recognized in Japan; it has been studied and used for treatment of heart disease since the 1970's.[27] In the last decade, use of doses circa 400 mg and above yielded remarkable results in a number of conditions[28] including cvd (eliminating the need for cardiac surgery and even heart transplant in many patients), cancer (complete recovery of stage 4 breast cancer), stroke recovery in humans[28,29] and in 3 animal models,[30,31] improvement in AIDS patients, etc.[28] Recently, Q10 was found safe and well tolerated by Parkinson's Disease patients at dosages of up to 1200 mg/d.[33] It slows the progressive deterioration of function in Parkinson's Disease and the benefit was greatest in subjects receiving the highest dosage. Q10 has been shown to be safe and effective in nine placebo-controlled large scale international cvd trials. It has no known toxicity or side effects.[28] Ischemic reperfusion injury (IRI) in various organs, especially brain, heart and kidney has recently been cited as a major cause of death in developed countries.[32] Exceptional protection obtained with Q10 in three animal stroke models was over twice any other agent tested in both pre- and 4-hour post-stroke treatment.

We have been engaged in a program designed to accelerate evaluation of Q10's remarkable efficacy in animal and human studies of a wide variety of disorders. We were serendipidously able to recognize, analyze, and report on surprising recoveries from hemorrhagic strokes due to accidental traumas in two patients.[28,29] The first patient's injury (and recovery) coincidentally followed a month of Q10 at 400 mg/day for memory impairment. In four weeks post-stroke, she progressed from coma through hemiparesis to complete recovery, indistinguishable from her premorbid condition, with no new detectable neurological deficit. Such therapeutic amounts of Q10 (200-1200 mg/day) cannot be provided by dietary intake alone[34] and thus must be obtained by supplementing via oral or IV routes. A fraction, possibly 10% or less, reported difficulty raising blood Q10 levels orally. We were able to analyze this problem and offer a method to avoid the consequences of ingesting Q10 during hypochlorhydria (see Oral Q10 and CanDPJ Revisited).

### Optimizing Antioxidants in Treating Infections

High ascorbate is necessary for CMI and requires proportionally high alpha-tocopherol to prevent hemolysis. (http://faculty.washington.edu/ely/JOM4.html) These needs have been well met in a trial Maier et al have designed and completed using intravenous ascorbate in critically ill surgical patients. Prior to this trial such patients had very high mortality in the ICU. Five-hundred and ninety-five patients (91% victims of trauma) were enrolled and analyzed. Those receiving antioxidant supplementation (alpha-tocopherol and intravenous ascorbate, 1 g every eight hours) had significantly reduced morbidity and mortality, especially less development of MOF (57% lower incidence) and shorter ICU stay. The authors concluded even greater benefits might be obtained if an approved IV-alpha-tocopherol existed. (Nathens et al.[17]). It seems plausible if: (1) ICU care Directors in some large facilities incorporate even the protocol of this first trial as routine; (2) the savings in lives and costs will compel all ICU's to adopt the

method; and (3) make it the de facto standard of care and accelerate development.

**Candida Relevant Properties: *The Amazing Work of Drs Iwata, Saifer, et al.***

Chronic Candida infection is commonly associated with CMI suppression, polyendocrinopathies and multiple hypersensitivities.[35,36] The microbiologist Kazuo Iwata: (1) discovered several high and low molecular weight toxins produced by Candida; (2) demonstrated their responsibility for the resistance of Candida to eradication; and (3) showed Candida's ability to disorganize bodily functions and produce symptoms of almost every known disease. He determined the physical and chemical properties of the toxins, demonstrated mechanisms in animal models, and published extensively.[18,37,38] The work of Iwata has been described in detail with a listing of his many papers.[38] The endocrinologist Phyllis Saifer summarized Candida's effects in producing (via Canditoxins) ~40 "pseudo" disorders (allergic, cognitive, endocrine, immune, metabolic, psychiatric, etc.).[38,Ch20] These scientific studies of Canditoxins, their mechanisms, etc, lie uncited, presumably unread like so much else. The true cause (i.e., candidiasis) of these "pseudo" disorders is almost never identified. Thus, no diagnostic data accumulate to justify the adoption of the BSAC plan or any other to end the tragic toll of candidiasis.

**Lethal Synergism of Candida and Bacterial Infections**

The microbiologist Eunice Carlson demonstrated in mouse models a very strong synergism between Candida and pathogenic bacteria including *Staphylococcus aureus* from toxic shock syndrome patients.[39] She demonstrated that, in simultaneous challenge with both agents at a dose far lower than the tolerated one of either agent, the *C. albicans* enabled the *S. aureus* to cause 100% mortality in the mice. Because of the vaginal ubiquity of *C. albicans,* this study is suggestive re toxic shock syndrome from trace contamination by certain strains of *S. aureus.*

**Candida Receptors for Human Hormones**

In the 1960's, Fudenberg et al demonstrated that Candida seemed stimulated when certain hormones were elevated including progesterone, estrogen, adrenocorticotrophic hormone, etc.[35,36] In the 1970's, Feldman and his coworkers at Stanford established that *C. albicans* in fact did have hormone receptor systems that resulted in exceptional growth stimulation.[40] This feature of Candida is responsible for predispositions to candidiasis in some people via endogenous and exogenous hormones such as contraceptive and steroid formulations, etc. The result is that antifungal therapy can not provide lasting relief for the patient on such medications until they are discontinued.

**Hyphal Forms of Candida**

In the absence of sufficient biotin (necessary for budding yeast forms), dimorphic yeasts convert to hyphal forms producing invasive candidiasis. In the colon, this process results when prolonged broad-spectrum antibiotic therapy decimates the normal bacterial flora that synthesize biotin at levels 20-fold above those needed for both Candida and the host.[41] Initially, as the killed bacteria vacate binding sites, a Candida population with doubling times of 10 hours expands to take over these sites on the colon surface. When the increased requirement for biotin by this population growth exceeds the declining production, the Candida convert to the invasive hyphal forms that secrete Candida proteinase and penetrate the colon mucosal surface. The resulting permeability can allow serious intoxication by bacterial cell wall fragments, and Candida toxins described above, etc, leaking from the colon.

**CanDPJ and Fungal MOF**

Even more dangerous is CanDPJ, which can arise from a number of scenarios. One "silent invasion" results because more than half of the oral flora frequently are Candida which survive passage through a stomach rendered hypochlorhydric by any of several means, as described above, and reach the DPJ. In the DPJ, growth of Candida may be stimulated by Q10, and then all convert to hyphal form (because of the lack of biotin), perforate and or penetrate (via Candida proteinase), colonize the region just below its mucosal surface and proceed to invade all organs contiguous to the DPJ. The collective effect causes regions in organs adjacent to the intestine (e.g., liver, pancreas, etc) to fail. Such a population of Candida would not be seen by endoscopy or culture and is not sensed as a septicemia. This fungal MOF may be so lethal because the patient is "essentially dead" (ie, beyond recovery) before explosive organ destruction (prevented by death) could have spilled sufficient Candida into blood to make the diagnosis clear. The most seriously ill such as ICU patients suffer a high incidence of this fatal fungal MOF. A large fraction of non-ill hypo-chlorhydrics may not experience the Candida conversion that leads to MOF but are at much greater risk for it. High M&M in hypochlorhydral patient classes such as described in the following paragraphs illustrate the danger of CanDPJ:

(1) Cancer. Numerous factors predisposing to candidiasis in tumour patients include immune suppression, surgery, recurrent antibiotic administration, intravenous catheters, hypertonic glucose solutions, chemotherapy effects including tissue damage and neutropenia. Candida is a common cause of death in cancer,[38] especially reaching 30% in some large studies with nonsolid tumours.

(2) Surgery. In addition to the risk factors for cancer, surgery patients include subpopulations with high initial mortality, especially in intensive care units. The great increase in surgery-associated fungal infections in the past decade has been well reviewed and need expressed for systematic management such as the BSAC proposal.[14,15]

(3) Burn. Candida infection in burn patients has increased substantially.[38,p339] Mortality ranges from 14% to 90%. There is a gradual increase in the frequency of candida infection in burn patients as time from admission increases.[4]

(4) Transplant. In candidates for liver transplant, 86% of the duodenal aspirates contained Candida. A positive culture from the stomach was a reliable predictor of the presence of Candida in the duodenum ($P = 0.0001$), a positive culture at any other site did not predict the presence of Candida at yet another site.[42,43]

(5) Central Nervous System (CNS). In many cases, the physical and neurological disorganization produced by CanDPJ results in chronic CNS derangement instead of proceeding rapidly to MOF and death. In these patients the large candida populations and their toxins result in a host of complex diseases. Numerous investigators have theorized and or demonstrated that various cognitive and neurological disorders are induced by infectious agents, multiple vaccine antigens, or other intoxications. These disorders include Alzheimer's disease, autism, chronic fatigue syndrome, epilepsy, schizophrenia, etc.[44] The agents have included HHV-6, other viruses, Canditoxin, and especially mercury from high copper amalgams (inhibits enzymes of CNS, CMI, etc.[38, p297,45]). The intestinal absorption is greatly increased due to methylation of amalgam mercury by oral flora,[45] an intoxication that can be significantly reduced by strict oral hygiene (until the amalgams are removed). One proposed mechanism in which dehydro-ascorbate (DHA), generated in the reduction of histamine (or in other reactions) causes smooth muscle spasms in the brain, an allergic dysautonomia, and a mottled blood supply visible on PET scans (Ely 1978

unpub; inspired by a remark of Hoffer re DHA in schizophrenics).

**Oral Q10 and CanDPJ Revisited**

All living cells require quinones in bioenergetics. Lower life forms such as *C. albicans,* are often able to alter the configuration of human ubiquinone (Q10) to produce their own forms usually by cleaving off some of the 10 isoprene sidechain units; some fungi eliminate the double bond in the last isoprene; etc.[46,47] Q10 thus altered by microbial or other parasitic forms cannot be utilized by the host. This loss may be very relevant to the high morbidity and mortality associated with colonization of the proximal gastrointestinal tract by Candida in several patient groups (as stated above) and suggests that malabsorption of orally administered Q10 might occur in patients having jejunal colonization by *C. albicans* or other Candida species. Topical colonization of small intestinal mucosa is opposed by shedding in healthy adults, but occurs in patients with various diseases. In addition, as stated earlier, when the dimorphic yeast, *C. albicans*, reaches the jejunum, it converts to its hyphal form due to low biotin levels, and then invades tissue below the normally shed layer.[38,48]

Occasional patients who do not absorb Q10 have been observed.[19] One such subject is an interesting paradigm. In him, we investigated the hypothesis that colonization of the proximal gastrointestinal tract by Candida species is a possible cause of lack of effect of orally supplemented Q10 (due to its uptake by candida). He had shown no significant rise (i.e., <10%) in blood Q10 from a baseline of 0.95 ppm after 1 yr on 800 mg/day. One half this dose should have elevated blood Q10 over 300%. In this non-absorber with persistent upper gut colonization (secondary to hypercorticism and antibiotics), *C. albicans* was 4+ in stool and anti-Candida albicans IgG was grossly elevated (>500 vs 60 normal, Immuno Diagnostic Laboratories, San Leandro, CA). Following surgical debridement of a slowly healing injury of his right foot dorsum, *C. parapsilosis* developed at the site, intractable to antifungals, and was progressing to necrotizing fasciitis. Amputation was contemplated by his surgeons. At this time, he ingested one Candida Transfer Factor capsule on each of four consecutive days. Within two weeks the lesion healed and was culture negative for all fungi. Endoscopy biopsies showed no Candida species on the gastric mucosa or duodenal bulb. The patient developed a positive delayed hypersensitivity skin test for *C. albicans*. At follow-up, seven months later, the lab was unable to grow Candida from fecal or saliva samples. The patient resumed oral Q10 at 400 mg/day and in a few weeks blood levels of Q10 rose 250% to 2.4 and 2.5 ppm measured by two labs (in close agreement on split aliquots from the same draw).

**Regimen Components**

This result supports the hypothesis (Ely, unpublished) that monilial colonization of duodenal and jejunal mucosal tissues might prevent treatment of Q10 deficiency states by oral supplementation of Q10. This patient subsequently adopted several preventive modalities including: (1) the use of antifungal mouth rinses (containing cetylpyridinium chloride) to reduce oral fungi;[49,50] (2) dosing with high-allicin garlic capsules, raw garlic, and time-release caprylic acid ("Mycopryl 680" capsules or powder, T.E. Neesby, Inc. Fresno, CA 93720) to minimize reinfection of the DPJ; and (3) use of biotin supplementation to prevent conversion of Candida to the invasive hyphal form. Coenzyme Q10 supplementation continued and blood levels were measured 2 years later and remained above 2 ppm. Also, blood analyses for Candida antibodies and antigen were in the normal ranges. These results suggest that the prophylactic modalities were effective in this subject. Prevention of esophageal perforation and invasive candidiasis by dimorphic

Candida spp in critically ill ICU patients may require antifungal treatment with polyene or imidazole derivatives, etc.

## Conclusion

Education of the public and medicine must be expedited re: (1) the existence of various candidiasis scenarios such as CanDPJ that predispose to high M&M; (2) hypochlorhydria (and its many causes including stress, otc PPI's, etc) as a major and most common risk factor for fatal candidiasis; (3) a number of other risk factors including recurring or prolonged administration of antibiotics, antacids, hormones, etc; (4) diagnostic methods for Candida including history, endoscopy, serology and culture; and (5) existing therapeutic and prophylactic antifungals, diflucan, CPC and time-release caprylic acid (Mycopryl 680 above), etc. It would appear that appropriate warning labels on PPI's and possible removal of their otc status could minimize one of the major risk factors for fatal CanDPJ via "silent" MOF. For additional detailed information, new developments, and answers to reader's questions see http://faculty.washington.edu/ely/jomof.html

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For a more complete view of the Candida threat, physicians should study PubMed using search terms including "Candida" with one or more of the following: age, esophageal perforation, MOF, mortality, and or other terms.