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To Whom It May Concern:

CFS is a complex, chronic illness of unknown cause. There is, however, mounting scientific evidence of immunologic, neurologic, metabolic and circulatory dysregulation in defined cases of CFS.

Clinically, CFS is a chronic, often debilitating disorder characterized by a triad of fatigue (with post exertional exacerbation), pain and neuropsychological complaints. The often severe cognitive problems and post exertional fatigue distinguished the syndrome from other, probably related disorders and often appear more prominently later in the evolution of the disease.

Early evidence of striking activation of the 2-5A, RNAse-L antiviral pathway[1] in CFS patients, and not in healthy controls, has supported the existence of a persistent, TH1 immune activation state. Increased 2-5A, RNAse-L expression also links the syndrome to increased expression of alpha-interferon as well as other immune cytokines and their clinical consequences. Among the consequences is an increased likelihood of allergic responses, which can be impressive in some including high histamine release and anaphylaxis. Many patients seem to benefit from antihistamines including benadryl (H1 blocker), low dose Doxepin Elixir (H2 blocker) and Pepcid (H3 blocker).

There are a group of commonly used anesthetic agents that are known histamine-releasers and are probably best avoided in CFS patients. This group includes the thiobarbiturates such as sodium pentathol, which is probably the most common induction agent, but is a known histamine-releaser. In addition, there are a broad group of muscle relaxants in the Curare family, namely Curare, Tracrium and Mevacurium, which are also potent histamine releasers and should be avoided in CFS patients.

Many patients with this syndrome are known to have intracellular magnesium[2] depletion, which can be confirmed by single cell electron beam x-ray spectroscopy, RBC magnesium or magnesium loading tests. For this reason, I would recommend all patients by given magnesium sulfate 50% solution, 2cc or 1 gram, IM 24-48 hours prior to surgery. Serum electrolytes and magnesium as well as a liver panel and a random serum cortisol should be checked prior to any general anesthesia. Intracellular magnesium depletion could result in untoward cardiac arrhythmias during or after anesthesia. For local anesthesia, I would recommend using Lidocaine without Epinephrine or if necessary, then sparingly @ 1% Epinephrine with Lidocaine.

In surgery requiring general anesthesia, I would recommend that potentially hepatotoxic anesthetic gases not be used including Halothane. Some patients with Chronic Fatigue Syndrome are known to have re-activated herpes group viruses (EBV, CMV, HHV-6), which may produce mild and usually subclinical hepatitis with slight serum liver test elevations. Hepatotoxic anesthetic gases may then provoke fulminate hepatitis in these patients.

In earlier studies by a cardiology group at John Hopkins[3], some CFS patients and especially younger patients demonstrated positive tilt table tests for neurally mediated hypotension (NMH) as well as other evidence of orthostatic intolerance (OI). OI and especially NMH can include a heightened reflex parasympathetic tone and induce hypotension and syncope in response to catecholamines such as epinephrine[4]. In addition, these patients, as a result of chronic neurogenic vasodepression associated with NMH specifically and OI in general, have chronic low blood volumes. Care should be taken to give these patients adequate hydration prior to surgery. Care should also be taken with drugs whose effects are potentiated by low blood volumes[5].

In more seriously ill CFS patients, I would recommend a 24-hour urine free cortisol both before surgery and in the post-operative period, if clinically indicated, to screen for relative cortisol insufficiency for which they are at risk[6]. Some patients may need brief steroid support during and after surgery if their 24-hour urine free cortisol is below 20-30 mcg/24 hrs.

Some years ago, Patrick L. Glass, MD., an anesthesiologist located in Reno, Nevada, has had considerable experience in administering anesthesia to CFS patients. He notes that prior to surgery, he performs skin tests for all the agents he may be considering for use with the patient. With CFS patients, he recommends Diprivan (propofol) as the induction agent; Versed (midazolam), Fentanyl and Droperidol during the anesthesia; and a combination of nitrous oxide, oxygen and Isoflurane (commonly called Florane) as the maintenance agent.

Finally, recent studies by Peckerman et al[7] show poor supine cardiac output (3-6 L/min) in disabled CFS patients (Normal = 7.0 $\pm$ 0.5) with preserved ejection fraction. We have accumulated evidence of diastolic dysfunction in 97% of CFS patients by one or more of three criteria. Poor pre-load will exacerbate diastolic dysfunction and place the patient at risk for a drop in pressure as well as NMH. We have also, in this clinic, found evidence of increased sensitivity to oxygen toxicity, especially at an FIO2 above 40%. However, at lower oxygen levels (below 30% FIO2) there appears to be greater tolerance in most but not all CFS patients. The etiology of this positive and negative sensitivity is likely to involve the metabolism of reactive oxygen species (ROS) which we have reason to believe is impaired. To quickly assess oxygen toxicity, we recommend that the breathing rate (breaths per minute) be measured and if an increase in rate is observed (panting) or a decrease in rate with associated alteration of consciousness (narcosis) is observed, then the patient is clinically toxic to oxygen. Venous blood gases but not arterial blood gases are almost universally abnormal with low P_vO_2 (<30) and usually high P_vCO_2 (>50). This is probably related to low cardiac output. We also have evidence of an increased chance of a PFO (~90% chance) with right to left shunting and therefore places the patient at risk in certain surgical settings, especially neurosurgery. This increase in PFO is likely related to oxygen toxicity and its physiologic consequences. Finally, pulse oximetry, while normal, shows a failure to desaturate after prolonged breath hold suggesting a functional left shift on the oxy-hemoglobin dissociation curve. Again, this may be linked also to low cardiac output and the patient may be maximally offloading to compensate at the microcirculatory level.

I hope you will find these comments useful and that they may serve to reduce the risk of surgery.

Sincerely,

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