

## THE HEART OF THE MATTER: CFS & CARDIAC ISSUES

### PART 2B

(current as of 04/02/05)

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#### PROTECTION FROM THE DEATH SPIRAL

So to protect yourself from going down the death spiral, your body stops making energy – at least to a point. That results in significant reduction of superoxide, and knocks out peroxynitrite. Thus, you cannot and will not advance [toward the event horizon], or, if you do, you will advance very, very slowly. I couldn't do that, and therefore I crossed the event horizon and almost died.

By the way, all this is Dr. Pall's model. The only added dimension here is the NMDA receptor, which sits on a neuron and when activated, triggers nitric oxide production. So blocking NMDA reduces nitric oxide.

[BACK TO PART 2A](#)

[GO TO PART 1A](#)

[GO TO PART 1B](#)

[BACK TO CHENEY TOPICS](#)

[USEFUL DEFINITIONS](#)



Search [MedlinePlus](#):

Search

#### KLONOPIN/NEURONTIN

**Patient asks:** "Klonopin only upregulates the GABA receptor, is that right?"

**Dr. Cheney responds:** "Yes. But that has an indirect effect on the NMDA receptor, through the GABA receptor. By upregulating [increase a response to a stimulus] GABA, you downregulate NMDA and reduce nitric oxide." [Thus, Klonopin and Neurontin can help reduce nitric oxide.]

#### AVOID PROVIGIL: IT STIMULATES NITRIC OXIDE

"Provigil does the opposite. Provigil does several things, but is mostly an NMDA-activator – it's a stimulant similar to cocaine – it will actually stimulate nitric oxide production. It may also stimulate ATP generation, which is the benefit perhaps that one sees. With more nitric oxide, you can think better, your memory improves, you can focus better, and you have more energy. But what you're doing is generating more peroxynitrite and this may not be felt for a while, but ultimately it's probably felt – in the brain at least – as Alzheimer's or Parkinson's Disease or worse, ten years from now."

#### HOW TO BLOCK PEROXYNITRITE

##### 1) INCREASE CO<sub>2</sub>

Let's turn to peroxynitrite. According to the Textbook of Medicine, and Dr. Pall himself, what is your primary scavenger of peroxynitrite? The answer is CO<sub>2</sub>. Carbon dioxide. When ATP is generated in the mitochondria, CO<sub>2</sub> is produced as a by-product. So, when you make energy [ATP], you produce the very thing needed to scavenge peroxynitrite. It's a beautiful system! When everything works perfectly, you can make a lot of ATP because superoxide is being broken down into water. And CO<sub>2</sub> is produced which will get rid of any peroxynitrite that accidentally happens to be produced.

What a great system! If that system could be maintained in the state it was in when you were born, you should live to 120 to

140 years of age. It's just that things creep in that degrade that operation, that system, and we just exit out earlier than we should.

Now, if you keep lowering ATP production, which then reduces the amount superoxide produced, you also reduce the production of CO<sub>2</sub>. "The result is you have less and less primary defense against peroxynitrite. It's a vicious cycle. And especially in the lowest energy states of all you really have that problem."

How do you increase CO<sub>2</sub>? Well, first let me ask how you decrease CO<sub>2</sub>, which we definitely don't want! Hyperventilation. If you hyperventilate, you dramatically decrease CO<sub>2</sub>, which would be highly damaging. It can produce carpal-pedal spasms in some patients (carpal: wrist; pedal: foot). Its most damaging effect is to your brain, however.

**REBREATHING:** You can increase CO<sub>2</sub>—and stop hyperventilation—by rebreathing. By inhaling your expired CO<sub>2</sub>, you actually scavenge peroxynitrite. [Rebreathing involves cupping your hands over your nose and mouth so that when you exhale, your CO<sub>2</sub> is trapped there and then you inhale it. Do this for a minute at a time, about once every four or five minutes during a thirty-minute period once or twice a day. You can also do this while breathing oxygen through a nasal cannula. Rebreathing can also help address respiratory alkalosis, *extremely common in CFIDS*, thereby improving microcirculation by shifting blood pH—thus allowing more oxygen to be transported off the hemoglobin.]

**KLONOPIN:** Taking Klonopin knocks out Nitric Oxide Synthetase (NOS) and that defends against peroxynitrite. Klonopin can also slow the breathing and that will raise CO<sub>2</sub>.

**BAROMETRIC PRESSURE:** Another way to do it is to walk in Death Valley. Below sea level, with all the extra oxygen, you hypoventilate and that will increase CO<sub>2</sub>. [hypoventilate: breathe abnormally slow and shallow] The opposite is flying in aircraft at 10K feet, causing you to hyperventilate, so flying in airplanes is not good. CFIDS patients often feel bad when low pressure comes through their area and they ache, among other things. Low pressures are like climbing to high altitude, and you don't do as well, because you tend to hyperventilate more.

## 2) URIC ACID

Uric acid is a powerful scavenger of peroxynitrite. Uric acid levels in CFIDS patients are among the lowest I've ever measured, in all of medicine. [Keep in mind that before specializing in CFIDS, Dr. Cheney served as a Major in the Air Force Medical Corps and was Chief of Medicine at Mt. Home Air Force Base hospital in Idaho for several years before moving on to a private practice in Internal Medicine at Incline Village, Nevada. He was also the Chief of Medicine at the Lakeside Community Hospital in Incline Village, Nevada. In Charlotte, before opening his own CFS clinic, he was the Senior Staff Physician in the Department of Internal Medicine at The Nalle Clinic.] CFIDS patients are the only ones you see at 1 or 2. Everybody else is up at 4, 5, and 6. Most CFIDS patients are quite low. The lowest I've ever seen as a group. [Dr. Cheney currently checks blood levels and 24-hour urine levels of uric acid.]

What do you make uric acid from? You make it from RNA and DNA metabolism and that is produced endogenously [within the body] and exogenously [outside the body]. Endogenous production is by apoptosis [normal, programmed cell death.] "Or by fasting in which you lose muscle mass or even by exercise which can produce muscle mass loss. In any event, you can produce your own endogenous RNA and DNA for uric acid production, which then scavenges peroxynitrite."

**SUSHI:** Exogenously there are certain foods you can eat that do it. [When considering the following foods, take your own food sensitivities and allergies into account!] The best foods that produce RNA and DNA are on the meat and the vegetable side. On the meat side, the best RNA and DNA production is in sushi. Sushi is very high in digestible RNA and DNA.

**Patient asks:** "Now what do you mean by sushi? Is that raw meat?"

**Dr. Cheney replies:** "Yes, raw meat. Raw meat of any kind is better than cooked meat." [Assuming it's safe and not contaminated.] Cooking destroys the RNA and DNA, depending on how much you cook it. If you overcook it, you definitely destroy it. But the most efficient way to destroy RNA and DNA is by microwaving.

**EGGS & RAW MILK (CHEESE):** Secondly, young food is better than old because it has a higher RNA and DNA content. How young can you go on the meat side before you can't go any younger? The egg. Eggs are very rich in RNA and DNA. And milk, if it's not pasteurized. It has to be raw milk. Raw milk has a high content of RNA and DNA. It also, interestingly, has a very high proportion of whey protein.

Moreover, if it's undenatured there's likely to be RNA and DNA embedded in that. So I have a sneaky feeling that part of the power of undenatured whey protein may in fact be its RNA and DNA. And if you could raise your uric acid level, you would allow yourself to make more energy, which will allow you to raise your Glutathione. That could well be the mechanism [of the effectiveness of undenatured whey protein].

Of course, raw milk is hard to deal in. There are laws against it. So how can you fix raw milk and make it legal? Make cheese out of it. Cheese made from raw milk and stored in caves—which is the traditional European methodology—actually saves raw milk in a form that can be stored for long periods of time, and has rich RNA and DNA content. You can go to most health food stores and ask for cheeses that are made from raw milk—that's what you want—and ask for the butter that is imported from France or Europe, which is also made from raw milk and is far better for you and is less processed.

**ISOPRINOSINE/IMUNOVIR:** There's a drug that raises uric acid called Isoprinosine or Imunovir. It's a very good immune-modulator; whose only potential side effect is an increase in uric acid levels. But that's not a problem for CFIDS patients! That "side effect" would have a profound ability to arbitrate this disease at its most fundamental level.

**SOY:** One of the highest RNA and DNA content foods on the vegetable side is soy. So, soy could be very helpful here. Be aware though that soy binds thyroxin [T4] in the gut and is problematic at best if you have hypothyroidism. [I buy frozen, shelled soybeans, let them thaw in the refrigerator, and eat them raw. Quick, easy, and, with or without salt, very good.]

**NUTS & SEEDS:** How young can vegetables be before they can't get any younger? Nuts and seeds!

**Patient asks:** "So baby lettuce and things like that?"

**Dr. Cheney replies:** "Yes, exactly like that." Young foods are better than old. Unprocessed foods are better than processed. Uncooked raw vegetables better than cooked. What is the best way to prepare raw vegetables? Juice them, especially if you have problems with digestion. Juiced raw vegetables, especially organic raw vegetables, would be very high in RNA and DNA content and would be quite easy to digest. Definitely, do not microwave them. Steam them or juice them.

### 3) CONSUME REDUCED CHOLESTEROL

HDL cholesterol binds peroxynitrite. When it binds peroxynitrite, it produces oxidized LDL. So LDL is what's left after having bound peroxynitrite, and HDL is what's ready to bind it. "So what you're looking at with cholesterol to HDL ratio, is actually how well you are in fact scavenging, or capable of scavenging, peroxynitrite."

It could be that you generate higher levels to protect yourself. When Anthony Komaroff looked at cholesterol in CFIDS patients, it was typically elevated. Which means, I think, that CFIDS patients may have an enhanced ability to scavenge peroxynitrite via the cholesterol pathway than a normal person does.

[Reviewing patient's lipid panel lab] Good, your HDL is high—77.6. Total cholesterol is not very high at 141. But your HDL is high, so this is a mixed picture.

**Patient asks:** "Which means? So what do I need to do?"

**Dr. Cheney replies:** "Well, you need to eat reduced cholesterol. What is reduced cholesterol? It's found in unprocessed cheeses, butter, and raw milk. When you process these things, you oxidize the cholesterol. [It's no longer "reduced".] If you don't have a source of exogenous cholesterol [i.e. the unprocessed cheese and butter made from raw milk, mentioned earlier], you excessively oxidize your own endogenous cholesterol. Both are bad —consuming processed forms of cholesterol and excessively oxidizing your own cholesterol.

The cholesterol elevation associated with Coronary Artery Disease (CAD) is not the cause of CAD; it's reflective of it. That's why treating cholesterol is a misapplication of therapy [statins] to the wrong thing [cholesterol]. You're treating your defense mechanism [cholesterol], as well as being in big trouble later down the road. Why? Because statin drugs lower CoQ10 levels. This generates yet even more peroxynitrite; at the very time, you're reducing your defense [cholesterol] against it [peroxynitrite].

That's a prescription for disaster. And you know what that disaster is in the published medical literature? People on statin drugs actually die of many cancers faster than people on placebo. The Harvard study said that in the New England Journal

of Medicine in 1996. This was also reported in animals on statin drugs. That's why, although there was a 3% improvement of death rate from CAD in the treated group, the net mortality was identical to the placebo group because those on statin drugs died of cancer more often than the placebo group. So there was no net gain. You just traded out what you died of. And if they'd followed the study out 10 years, they would have seen more Parkinson's disease. However, they ended the study at five years.

They have also seen rhabdomyolysis [destruction or degeneration of skeletal muscle tissue accompanied by the release of muscle cell contents into the bloodstream resulting in hypovolemia (decrease in the volume of the circulating blood); hyperkalemia (the presence of an abnormally high concentration of potassium in the blood); and sometimes acute renal failure] in all the developing statin drugs, resulting in one being recalled. I suspect rhabdomyolysis is involved by CoQ10 deficiency produced by the statin drugs.

### THREE WAYS TO BLOCK NITRIC OXIDE

#### 1) HEMOGLOBIN

The best endogenous scavenger of nitric oxide is hemoglobin. [Hemoglobin: the "red" in red blood cells—a protein that transports oxygen from the lungs to the tissues.] "When hemoglobin scavenges nitric oxide, the nitric oxide bends the hemoglobin, causing the red blood cells to deform. Dr. Les Simpson in New Zealand found that the red blood cells of CFIDS patients were deformed, and when they're deformed they can't get through the capillary bed very well and can cause pain."

"An indication of this [RBC deformation] is it also drops the SED rate. CFIDS patients have the lowest SED rates I've ever recorded, and the ones with the lowest SED rate may have the greatest degree of pain." [SED rate refers to sedimentation rate, and is listed as ESR on many lab tests.]

"Do you know what your SED rate is by chance? Normal for you would be 15 plus or minus five. That's according to the British literature. A female your age has a higher SED rate than children and males. And you're probably down around 0 to 3. Which means you have Nitric Oxide binding hemoglobin, and therefore you have an induced hemoglobinopathy [a problem with the hemoglobin—nitric oxide bends it], and red cell deformation, and a low SED rate on that basis."

In the Laboratory Textbook of Medicine, there are only three diseases that lower the SED rate to that level. One is Sickle Cell Anemia—a genetic hemoglobinopathy. The second is CFS—an acquired hemoglobinopathy (acquired by Nitric Oxide binding). And guess what the third disease with a low SED rate is? *Idiopathic Cardiomyopathy!*

The more deformed red blood cells you have, the more pain you may experience. It's bad enough when you don't perfuse your muscles and your joints [because of poor microcirculation], but it's even worse when your red blood cells are so deformed that they can barely get through the capillaries, or are blocked entirely. Some CFIDS patients have a problem similar to that of Sickle Cell patients in this regard, and Sickle Cell patients have unbelievable pain—you have to give them IV morphine and fluids. That's how they're treated.

#### 2) HYDROXYCOBALALMIN INJECTIONS (B12)

Another important scavenger of Nitric Oxide is B12—it binds Nitric Oxide quite vigorously. [This form of B12 is available from compounding pharmacies with a script from a doctor. One cc a day is recommended, at a concentration of 10,000 mcg/ml. The injection can be intramuscularly or subcutaneous. Some patients need to work up to this dose slowly since it also detoxifies you. Patients report more energy, less brain fog, better sleep. Some patients report a significant benefit at a higher dose, perhaps 2 cc's. I usually take one cc a day, but if I've done too much and am crashing, I take two cc's. It helps!]

#### 3) MAGNESIUM SULFATE INJECTIONS

Magnesium blocks the production of nitric oxide by calcium channel blockade. [Many patients benefit from magnesium injections, which are virtually painless with the addition of taurine. The Magnesium used by most is Magnesium Sulfate—standard 50% solution—1/2 cc drawn into the syringe first, followed by 1 1/2 cc's of Taurine. The Taurine is compounded at 50 mg/cc. The taurine makes the injection virtually painless and the ratio eliminates the hard knots many are

familiar with. The injection is intramuscular, given in upper, outer quadrant of either buttock. Both require scripts from a doctor.]

### OTHER TREATMENTS

Numerous other treatments are used by Dr. Cheney as appropriate with certain patients. Some of the more common ones are zinc and selenium supplements that help block mercury. [**Zinc Picolinate**: 50 mg, once a day; **Liquid Selenium** by Allergy Research Group: 1 tsp a day.]

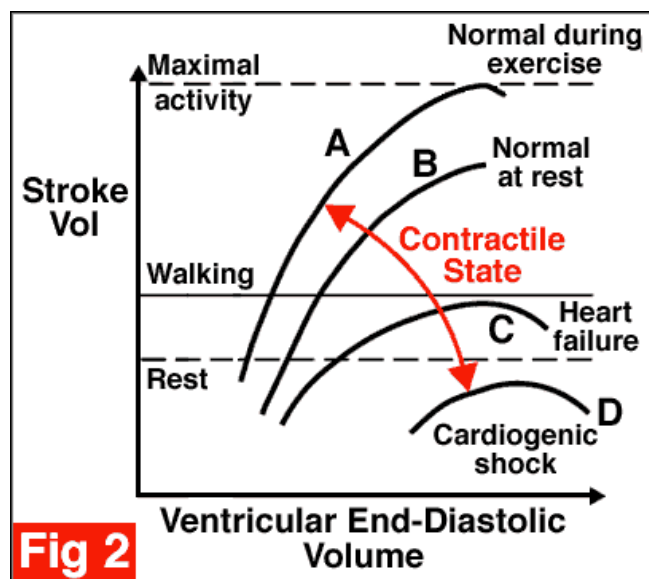
**CoQ10 and/or Idebenone.** Idebenone comes in 40 or 45 mg capsules, and one such capsule is roughly equivalent to 200 mg of CoQ10. [600 mg of CoQ10, or an equivalent combination of the two, is highly recommended. There is a lot of poor quality CoQ10 on the market —the cheaper products may not be worth your money. Douglas Lab's "CoQMelt" is a good product and is available from needs.com. Kirkman Labs sells Idebenone, kirkmanlabs.com. It's also available at some local health food stores—20% off on the first Tuesday of each month at Sunflower Shoppe in Fort Worth and Healthy Approach in Colleyville.]

**Proanthocyanidins or bioflavonoids.** The most powerful of these antioxidants are in Grape Skins or Pycnogenol. It just makes good sense to supplement with these.

**Essential Fatty Acids**, such as Fish Oil, Evening Primrose Oil, and Borage Oil. "I tend to recommend Fish Oil only. It has certain advantages over the others." [Tyler's Eskimo-3 liquid, one teaspoon a day, manufactured by Cardinova in Sweden.]

### PHYSIOLOGY: PRELOAD AND AFTERLOAD

Turning to physiology, how does a cardiologist treat the heart problem? He uses the Frank-Starling Curve. [Dr. Cheney drew a curve for his other patient that I don't have. See [www.nda.ox.ac.uk/wfsa/html/u10/u1002\\_02.htm](http://www.nda.ox.ac.uk/wfsa/html/u10/u1002_02.htm) for sample curves.]



[To understand this diagram and the rest of this section, the following somewhat simplified definitions may be helpful. Stroke Volume (SV): the amount of blood pumped by one contraction of the heart. Cardiac Output: the volume pumped out in one minute (SV x heart rate). The ventricle is a lower chamber of the heart. Oxygenated blood is ejected from the left ventricle to the body; unoxygenated blood travels from the right ventricle to the lungs.

Preload is the amount of blood in the left ventricle waiting to be pumped out to the body, or —as on the diagram—the volume in the ventricle at the end of diastole. It's mainly dependent on the venous return of blood from the body. Diastole is

when the muscles relax and a chamber of the heart expands and fills with blood; compared with Systole, when the muscles contract and expel blood from the chamber. Afterload is the resistance the blood encounters when ejected from the heart—remember how arteries constrict like nozzles?]

[The diagram could be seen as plotting the amount of blood waiting in the ventricle to go to the body (horizontal axis) against the amount of blood that is actually ejected from the ventricle (vertical axis). Four curves are shown, the highest two (A and B) being healthy hearts with good cardiac output during exercise and at rest. The lower two curves (C and D) indicate diseased hearts that cannot produce sufficient cardiac output. While they have lower cardiac output, they also have greater ventricular volume—there is more blood in the heart, but the heart muscle isn't strong enough to pump as much out. There are also three dotted horizontal lines at increasing heights indicating the necessary cardiac output for rest, walking and maximal activity.]

Dr. Cheney states, "This is the normal Starling Curve." [Presumably something like Curve B.] This curve is where most CFIDS patients are. [I suspect CFIDS curves are between B and C; i.e.—a curve not shown on this diagram.] The point at the top of that curve is the sweet spot. That would give you the most cardiac output and thus the greatest tissue perfusion, and that would be the best. On either side of that peak, the cardiac output goes down. Most CFIDS patients sit right here. [Probably somewhere on the left side of the curve.]

Now, here is a Congestive Heart Failure curve. [Curve C] Those patients are treated with Lasix to make them eliminate the extra volume, and then they are able to move up the curve and improve their cardiac output. "Most of you, on the other hand, need volume, and as we give you more volume you will come up onto the peak and will maximize your cardiac output. But, if we overshoot, you're going to go down the other side and you actually lose volume. And if you keep going down you'll actually go into heart failure." It's critical to understand the Frank-Starling Curve of Cardiac Output, where you [the PWC] are and how to manipulate it. [Notice that the healthy hearts in the diagram (curves A & B) have little to no drop after their peak!]

#### **PRELOAD: LYING DOWN**

How do you augment preload—which is blood volume—to improve cardiac output? You lie down. When you lie down, you increase the cardiac output a whopping 2 liters per minute. Don't sit, don't recline—lie down. Some patients need to lie down and augment volume anytime, all the time.

But, what if you're one of the ones right near the top of the curve and you increase your volume (preload) 2 liters by lying down? You could actually go over the peak and down the other side. Do you know what that means clinically? Some patients can't lie down! Some tell me, "When I lay down I cannot rest well or sleep." They went right over the top and dropped their cardiac output by lying down!

#### **PRELOAD CHRONOBIOLOGY: DAYTIME VS. BEDTIME**

There is a chronobiology to this curve: the time of day affects it. In the daytime, patients need to increase blood volume by taking in fluids. That allows them to be up more. But some can over treat by drinking fluids and lying down in the daytime. [Some with this problem who can't be up find a semi-recumbent position helpful. Use pillows to raise your torso.]

However, at nighttime, the opposite happens. The chronobiology drops your cortisol and aldosterone so you don't hold fluids as well, and all that combines to allow this type of patient to lay down without this problem. Patients with this problem (lying down makes them feel worse) should only expand volume in the first six or seven hours of their day with the Hydralate (Gookinaid) or Home Brew mentioned below, then switch to water. And if they lie down while over-expanding volume with Home Brew or other supplements or drugs, they'll get creamed. These patients should not use the Home Brew during the six or seven hours before bedtime. If they do, they may not be able to sleep.

#### **PRELOAD: HYDRALATE (GOOKINAID)/HOMEBREW**

"Volume loading using appropriate volume expanders can be quite helpful. This can be done in a variety of ways, but falls best under the term of isotonic [same salt concentration as normal cells and blood] volume expansion. Hydralate

(Gookinaid) is a well-documented isotonic volume expander and is used in athletic events such as marathon running." [Gookinaid.com] "It has an advantage of rapid absorption and is maintained in the intravascular volume far longer than hypotonic [less salt concentration] drinks such as water itself. The disadvantage to Hydralate (Gookinaid) is that it has sugar in it in the form of glucose."

"Another option would be a HomeBrew mixture of sea salt and "No Salt". [HomeBrew: one cup of filtered or spring water, 1/8 teaspoon of Sea Salt, and 1/8 teaspoon of "No Salt" salt substitute (potassium). Add lime juice or an herbal teabag as well as stevia for taste.] Four to eight glasses of Hydralate (Gookinaid) or HomeBrew are recommended.

Why is potassium in these drinks? Potassium induces Aldosterone , a hormone that significantly increases blood volume.

#### **PRELOAD: CORTISOL AS LICORICE ROOT**

For those with low blood pressure—most CFIDS patients have low blood pressure—cortisol could also be useful and can be improved adaptogenically using Licorice Root Extract at 1 to 2 tsp every other day. [Adaptogenic substances respond to what your body needs. I take licorice root capsules. Only the type with glycyrrhizin works for this purpose.]

#### **AFTERLOAD REDUCTION: MAGNESIUM**

The second thing you need to do after increasing your Preload, is reduce your Afterload. This means reducing the resistance the blood encounters. The best Afterload-reducing agent I know of is Magnesium, an adaptogenic vasodilator [opens up/relaxes the blood vessels as needed]. Magnesium and taurine injections have been very effective for many patients [see details on these injections in the earlier section]. You could also use oral Magnesium Glycinate capsules in the form of Magnesium Glycinate Forte 300 to 500 mg at bedtime. [I use both the oral and the injectible forms.]

Will implementing these treatment measures cure you? Absolutely not, because none of this is getting at the primary issue. It is directed at what is most dysfunctional about this disease. If we're trying to get you functional, this is where we start.

*[This concludes the information on CFS and Cardiac Issues. Look for future articles on other topics. Dr. Cheney will speak on this topic on June 18 in Irving, TX. His presentation will also include new information on CFS and Diastolic Cardiomyopathy. See [www.virtualhometown.com/dfwcfids/menu.html](http://www.virtualhometown.com/dfwcfids/menu.html) for details about the seminar and information on ordering a videotape.]*

[BACK TO PART 2A](#)


[BACK TO PART 1A](#)

[BACK TO PART 1B](#)

[BACK TO TOP OF PAGE](#)

[BACK TO MAIN RESEARCH PAGE](#)

[BACK TO DR. CHENEY TOPICS](#)

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[BACK TO TOP OF PAGE](#)

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