

# Escape from the Acidic Tumor Microenvironment

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***By Eugene L. Heyden, RN***

“The biggest weakness of current cancer treatments is that they only treat the cancer and not the actual patient.” ~ **Wada et al., 2022**

*“The Warburg phenomenon, with the attendant acidification of the extracellular*

*milieu of tumors, has fascinated cancer scientists for many decades, but the modulation of these phenomena has yet to earn a role in orthodox cancer therapy.”*  
~ **McCarty and Whitaker, 2010**

*“Malignant tumors exhibit an increase in glucose metabolism when compared to normal tissue. The increased metabolism generates an acidic tumor environment, which promotes local invasion, metastasis, and inhibition of immune surveillance.*

*“Export of acid by solid tumors has been shown to degrade both the extracellular matrix and be toxic to normal tissue in the vicinity of the tumor. This destruction of surrounding tissue and re-modeling of the extracellular matrix provides the conditions necessary for local invasion and metastasis of tumor cells.*

***“Tumor acidity can be neutralized with oral buffers, reversing some of the sequelae of acidity, including local invasion, metastasis, and immune inhibition.” ~ Pilot et al., 2018***

*“In recent years, sodium bicarbonate ( $\text{NaHCO}_3$ ), a simple inorganic salt, has been found to be able to reverse the pH of tumor microenvironment and inhibit the invasion, metastasis, immune evasion, drug resistance and hypoxia of tumor cells. Thus,  $\text{NaHCO}_3$ -based therapy is a potential approach for the treatment of cancer, and the related studies have been increasingly reported.” ~Wang et al., 2021*

It certainly sounds bad, and certainly it is—a tumor microenvironment (of acid) that **1)** acts to destroy surrounding tissue; **2)** promotes tumor invasion and metastasis, and **3)** prevents the immune system from knowing what is really going on . . . and acting with vengeance. In our treatment of cancer, one would think that addressing the acidic tumor microenvironment, head-on, would be Job 1. Something tells me, when it comes to present-day cancer therapy, addressing the acidic tumor microenvironment is not on the agenda. (see Koltai, 2020). Given all we know, I find this quite surprising.

I suppose you are wondering, “Where is all the acid coming from?” We have known the answer since the 1920’s (Liberti and Locasale, 2016). A scientist named Otto Warburg discovered that the cancer cell, hence the tumor, continually discharges large amounts of lactic acid into the surrounding microenvironment due to a high

rate of glucose utilization (Liberti and Locasale, 2016). And because of reduced blood flow in the tumor microenvironment, the acid persists and is not easily removed (McCarty and Whitaker, 2010; Yang et al., 2020). This phenomenon, which appears to be operative in all cancer types (Wada et al., 2020), is known as the Warburg Effect or Warburg Phenomenon. The high rate of glucose utilization, leading to a high rate of lactic acid production, benefits the cancer when it is promptly exported out of the cancer cell and into the tumor microenvironment, but does not benefit the individual involved.

Why the Warburg effect should be targeted is rather simple. The acidic microenvironment allows the tumor to

- Evade the immune system, effectively creating a zone of protective immunosuppression (Faes and Dormond, 2015; Pilot et al., 2018)
- Create a unique microenvironment that supports the growth needs of the cancer cell (Faes and Dormond, 2015)
- Convert the regional macrophage, an immune cell that ordinarily takes up residence within the tumor, from a cancer-fighting M1 type into a cancer-supporting M2 type (Ibrahim-Hashim and Estrella, 2019)
- Degrade the extracellular tissue environment, allowing cancer cells to spread and to metastasize (Faes and Dormond, 2015)
- Directly kill normal, surrounding cells (Ibrahim-Hashim and Estrella, 2019)
- Block the uptake and effectiveness of various chemotherapeutic drugs (Hamaguchi et al., 2020)

But there is good news here: ***“The pH paradigm of cancer is the disease’s weak spot. A rational approach to targeting the weak spots of cancer should be highly rewarding, if at the same time this targeting is not toxic, is well tolerated by patients and is available at very reasonable costs.”*** (Koltai, 2020)

And we’re in luck! It looks like we have located someone who found the weak spot and took advantage. And as far as we know, he is still doing quite well (and perhaps is still alive). But before we get to the story, keep this in mind:

*“If one patient can do it, there’s no reason others can’t. I realized that medicine has been studying its failures when it should have been learning from its successes. We*

*should be paying more attention to the exceptional patients, those who get well unexpectedly, instead of staring bleakly at all those who die in the usual pattern.”*  
(Siegel, 1986)

## **Case report**

*“Several in vivo and in vitro studies have demonstrated that tumor acidity can be altered through bicarbonate administration, and suggested that systemic buffering may lead to antitumor effects.” ~ Hamaguchi et al., 2020*

This is the story of a 79-year-old gentleman whose kidney cancer with mets to the liver would just not go away. Indeed, first-line treatment failed him, and he took matters into his own hands. According to the report:

*“. . . in Supplementary data, we include the experience of a 79-year-old man with widely metastatic renal cancer at the Moffitt Cancer Center. After failing first-line treatment, he discontinued conventional therapy and began a self-administered course of vitamins, supplements, and **60 g of bicarbonate** mixed in water daily. As of this submission, he has remained well with **stable tumor for 10 months.**”*  
(Silva et al., 2009)

As we look a little further into the supplementary data, the gentleman of our story was first diagnosed in January 2004 with a large right renal cancer with a blood clot extending into his inferior vena cava (a large vein leading to the heart). In February of 2004 the right kidney was removed as well as the blood clot. A year and 1/2 later, June of 2005, it was discovered that the cancer had metastasized to the liver, in subcutaneous tissues, and in his retroperitoneal lymph nodes. This leads us up to September 2007.

*“In September 2007 he elected to discontinue all conventional therapy and began a self-administered regimen of vitamins, supplements, and 3 “heaping tablespoons” of sodium bicarbonate in water per day (about 60 grams total). As of the date of this submission, he has maintained this therapy with no complications. His weight is stable. He walks 2 miles every day and had cataract surgery in March 2008 without*

complications.” (Silva et al., 2009)

And there is more:

*“Interestingly, the tumors that were necrotic in the initial scan became much less so on the follow-up study. At the time of this submission the patient remains clinically well.”* (Silva et al., 2009)

The experience of the gentleman of our story led to the following commentary:

*“The clinical feasibility of chronic ingestion of bicarbonate to reduce tumor invasion is an open question. Interestingly, NaHCO<sub>3</sub> is readily available in grocery stores (as baking soda) and in over-the-counter preparations for clinical use as an antacid. The recommended daily dose is five teaspoons a day, which is 25 to 50 g (depending on how heaped the teaspoon is). This dose has been administered chronically (i.e., >1 year) in patients with renal tubular acidosis and sickle cell anemia without adverse affects (sic).”* (Silva et al., 2009)

## **Putting it all together**

Our 79-year-old gentleman may have followed directions that were similar to the following:

*“Large acute doses of either sodium bicarbonate or trisodium citrate (which have been studied as aids to exercise performance, usually at 40-60 mg/kg) can induce temporary nausea and diarrhea; it therefore is prudent to administer the daily dose gradually throughout the day. Moreover, gradual administration should more aptly mimic the mouse study, in which sodium bicarbonate was administered in drinking water, and thus was consumed continuously during waking hours, presumably achieving a more even elevation of tumor extracellular pH than could be achieved with bolus doses. The protocols currently employed are: add 500 mL (about 2 cups) of water to a small teapot and stir in two rounded teaspoons (about 12 g) of sodium bicarbonate or trisodium citrate plus one packet of sweetener of choice. Patients who are “on the go” can prepare this beverage in a 500-mL water bottle. This is to be consumed gradually over an hour or more. If this procedure is followed three*

*times daily (e.g., in mid-morning, mid-afternoon, and late evening), about 36 g of sodium bicarbonate or trisodium citrate will be provided daily. If desired, this fluid can be heated to make tea or herb teas, or can be flavored with a Crystal Light™-type product.”* (McCarty and Whitaker, 2010)

But others, trying to put alkalinization therapy through its paces, have recognized that such a degree of sodium bicarbonate consumption is not at all realistic and may create complications, so why not combine sodium bicarbonate supplementation in lesser amounts, combined with an alkaline diet as a strategy to reduce the amount of sodium bicarbonate required? And why not use a urine pH test (easily done at home) to determine the advisability of bicarbonate supplementation? *“Oral bicarbonate (3.0-5.0 g/day) was given when urine pH did not increase above 7.0 or when patients wished to take it.”* (Hamaguchi et al., 2020)

### **A dietary approach: The Alkaline Tide Diet**

Recognizing that sodium bicarbonate supplementation, in quantities sufficient to effectively alkalinize the acidic tumor microenvironment, has poor compliance written all over it, dietary strategies have been devised. What follows is a synthesis of the several dietary alkalinizing or buffering strategies put forth by investigators working along these lines. I like to call it **The Alkaline Tide Diet**. That being said, and in full disclosure, The Alkaline Tide Diet is basically **The Buffer Diet**, introduced by Pilot et al in 2018. You might say, “The Alkaline Tide Diet is The Buffer Diet, reimagined.”

The Alkaline Tide Diet is constructed around a normal phenomenon known as “the alkaline tide.” The alkaline tide occurs when a relevant amount of protein is consumed during a meal and undergoes the process of digestion—and lasts for approximately an hour, maybe close to two (see Wikipedia, 2023). Importantly, the alkaline tide is a prolonged period of **compensated metabolic alkalosis** of the blood which can, in turn, diffuse away hydrogen ions that support the acidity of the acidic tumor microenvironment.

*“The buffer diet is used to induce compensated metabolic alkalosis through the use*

*of net-alkali generating sources to buffer the tumor pH while leaving systemic pH values unchanged. In compensated metabolic alkalosis, blood bicarbonate levels will increase based on the rate of bicarbonate reabsorption in the kidneys as  $H^+$  is excreted and this will increase the pH of the extracellular environment surrounding tumors.”* (Pilot et al., 2018)

Mechanistically, when the stomach is tasked to digest protein, a large amount of hydrogen ions are released into the lumen of the stomach, and all the while blood bicarbonate levels in the blood will correspondingly increase (Pilot et al., 2018). Important to the scheme of things, this temporary increase in blood bicarbonate levels, this metabolic alkalosis, this alkaline tide, can be extended by dietary and supplementary manipulation. And so as not to interfere with the objective, a baseline diet pattern is essential—why produce more acids for the body to deal with, more acids that will need to be neutralized and which will detract from the objective of The Alkaline Tide Diet? (see Ribeiro et al., 2013)

Fundamentally, such a diet would need to be low in meat and low in full-fat dairy and high in vegetables and fruits, in as much as *“Fruits and vegetables are known to have an alkalizing effect on urine pH, and meat has an acidifying effect on urine pH, as demonstrated from renal net acid excretion, which was calculated to predict the acid-base balance.”* (Hamaguchi et al., 2020) **Impressively, “In this study, we demonstrated that a urine pH of more than 7.0 was significantly associated with prolonged OS [overall survival] in advanced pancreatic cancer patients, compared with a urine pH of 7.0 or less.”** (Hamaguchi et al., 2020, emphasis added)

The best overall guide to dieting along these lines that I have been able to locate is **The PRAL Table** ([The-PRAL-Table.pdf \(inaturally.com.au\)](http://The-PRAL-Table.pdf(inaturally.com.au))). In all practicality, following a diet of 1/3 acid-forming foods along with 2/3 alkaline-forming foods is a good general health practice . . . period. But to be quite honest, many, perhaps the majority of the alkalizing foods listed in the PRAL Table do little to buffer acid at the cellular level. For that, you need a diet that includes foods with recognized buffering power. An excellent list of foods to consume and to avoid (within reason) can also be found on the last two pages of Ribeiro et al., 2013.

The Alkaline Tide Diet, as does The Buffer Diet, does allow meat products, but strongly suggests that they be meats low in cysteine and methionine (Pilot et al., 2018). In this context,

*“It is also important to consider not only the direct effects of buffering, but also the metabolic fate of the protein. It is well known that sulfur in proteins (cysteine, methionine) is oxidized to sulfuric acid, which adds to the acid load. Thus, sulfur-free (e.g. whey protein, pollock, turkey breast) or low sulfur proteins (e.g. nuts, peanuts, black beans, peanuts, cheese, soy) are often categorized as ‘non-acidifying’ whereas high sulfur proteins (i.e. sesame and safflower flour, beef, and bison) are ‘acidifying’.”* (Pilot et al., 2018)

Given that the alkaline tide is limited to 2 hours (or less) after each meal, The Alkaline Tide Diet includes interventions that prolong the alkaline tide, and thus provide a greater opportunity for hydrogen ions to be diffused away from the acidic tumor microenvironment. Such interventions prolong the state of metabolic alkalosis occurring from dietary protein digestion. Such interventions also decrease the amount of sodium bicarb one would need to consume in order to mimic the experience of our 79-year-old gentleman, showcased above. And doing so is not all that complicated.

The interventions suitable to prolong the alkaline tide, both after and between meals, include the use of protein snacks or protein supplements such as Vanilla Ensure, tablets such as Tums, and diluted sodium bicarb powder and/or sodium bicarb in capsule form. Such items can be assigned a buffer point to help keep you on track, with one point equal to 1 gram of sodium bicarb (Pilot et al., 2018). The recommended buffer points per day required to create an extended period of metabolic alkalosis is estimated to be 50 buffer points per day (Pilot et al., 2018). Obviously, 60 buffer points would also be a good goal to aim for.

## **A day in the life**

By way of example, and following the buffer point system of Pilot et al., 2018, a day in the life of someone who wants to strip away hydrogen ions from the acidic tumor



microenvironment, and doing so for an extended period of time during the day, might look a lot like this:

**Before breakfast**, added to a cup of coffee, is a can of Vanilla Ensure (**5.2 buffer points**).

For **breakfast**, two eggs (1 buffer point), a glass of low-fat milk (1.4 buffer points), and a banana (0.2 buffer points). So far, we are up to about **8 buffer points** for the day. And we are just getting started.

**Between breakfast and lunch**, we are going to do some serious supplemental buffering. How about 3 grams of calcium carbonate in the form of chewable Tums? (3 buffer points.) And since we need to drink a lot of water, how about we drink 2 glasses of water, either mixed with 3 grams of powdered sodium bicarb or 3 grams of the same in capsule form (spaced out during the water drinking period? (3 buffer points.) And just to make sure we trigger a new alkaline wave, let's consume a second can of Vanilla Ensure (5.2 buffer points). So, before lunch, our buffer point total is now up to **19 buffer points** for the day.

For **lunch**, how about a bowl of chili along with a serving of quinoa salad (estimated to be a total of 5 buffer points)? Add a glass of low-fat milk (1.4 buffer points) and a slice of Swiss cheese (0.7 buffer points) and we are up to **26 buffer points** for the day. Not bad!

**Between lunch and dinner**, let's repeat the Tums, bicarb and water routine we did earlier in the day (combined, 6 buffer points), along with another can of Vanilla Ensure (5.2 buffer points). This brings us up to about **37 buffer points** for the day. And we're not done yet! Surprisingly, we need only about 13 more points of to achieve our goal of 50 buffer points/day.

For dinner, it's a big bowl of lentils (7.2 buffer points); a glass of low-fat milk (1.4 buffer points); a tuna salad (estimated 1 buffer point), and another slice of Swiss cheese (0.7 buffer points). And with that, we have achieved a total of **47 buffer points** for the day. Now, only 3 buffer points left to reach our goal.

Sometime **after dinner**, we achieve our goal of **50 buffer points** by consuming 3 1-

gram tablets of Tums. But just to be sure, we achieved enough buffering during the day, we might as well sip on some flavored bicarb water or take a few extra bicarb tablets as we finish out the day.

Using this “day-in-the-life” template, one can achieve the goal of creating and expending a prolonged period of metabolic alkaloses—exactly what our 79-year-old gentleman did—and not have to suffer through the distasteful consumption of glass after glass of bicarb water each and every day.

## **General guidelines**

To increase the impact of the alkaline tide and the effectiveness of The Alkaline Tide Diet, here are the rules of the road:

- Secure the cooperation of and ongoing monitoring by a physician. Word of caution: *“In one case in 2012, for example, a 27-year-old British woman paid thousands of dollars to a doctor for alkaline treatment using baking soda (sodium bicarbonate), but after the treatment, her condition worsened due to severe alkalosis and soon afterwards she died.”* (Bahrami and Greiner, 2021) Consulting a dietitian is also recommended.
- Favor consuming protein foods that are less acidifying, e.g., vegetable proteins (particularly legumes such as lentils and kidney beans, and meats relatively low in cystine and methionine) (see Pilot et al., 2018; [The-PRAL-Table.pdf \(inaturally.com.au\)](#); Bahrami and Greiner, 2021).
- Diet should provide adequate amounts of protein with each meal to evoke a satisfactory alkaline tide. 15 to 20 grams of protein each meal should be sufficient, particularly so if between-meal protein supplementation is also being employed.
- Select before-, after-, and between-meal supplements that create and extend the alkaline tide, as outline above.
- Restrict or eliminate soda pop from the diet (Ribeiro et al., 2012).
- Limit dietary fat intake, selecting lower fat varieties of meat and low-fat instead of full-fat milk (Al-Dabbas et al., 2010; Pilot et al., 2018).
- Be mindful, there are *“Procedures and treatments that reduce acid output*

*also decrease the alkaline tide. ... Examples include vagotomy, H2-receptor antagonists, calcium channel blockers, and acetazolamide, a carbonic anhydrase inhibitor. The last study supported the direct correlation between gastric acid secretion and alkaline tide.”* (Raskin and Niv, 2015). In addition, PPIs (e.g., Prevacid, Prilosec) can effectively block the creation of the alkaline tide (Raskin and Niv, 2015).

- Caution should be exercised when promoting metabolic alkalosis by diet and supplements while at the same time taking medications such as certain diuretics (e.g., Lasix, Diural) ([ama-assn.org](http://ama-assn.org)). On the other hand, medications such as Lasix could be added to the dietary/supplement regime herein described, in order to reinforce and help maintain the metabolic alkalosis state. In which case, approval and careful monitoring by a physician would be in order.
- Be aware: Recommendations vary between authors regarding the buffering capacity or acid/alkaline producing propensity of various food items. This could relate to differing forms of analysis, the differences between acidifying/alkalizing effect and the hydrogen ion binding capacity of a particular food item, in addition to differing methods of food item preparation (see Pilot et al., 2018).
- Strict compliance recommended: “. . . subjects on buffer therapy should not consume foods that would counteract the buffer and inhibit therapy.” (Ribeiro et al., 2013)
- pH urine testing may be useful in monitoring the effectiveness of The Alkaline Tide Diet, with a goal of maintaining a urine pH of 7.0 or greater (Hamaguchi et al., 2020).

## **Me, too**

There are others besides our 79-year-old gentleman who have achieved success by taking measures to escape the acidic tumor microenvironment by dietary intervention. And I’m sure there are others.

*“Male, 84 years old (at the time of first consultation), Unresectable renal pelvis cancer, cT3N2M0, Periaortic lymph node (LN) metastasis (+) . . . He was told by the*

*doctor that anticancer drug treatment would not be given because he was too old, and it would not be effective. An alkalizing diet and intravenous vitamin C showed a marked improvement in the renal pelvis cancer. No anticancer drugs were used. After 4 months of alkalizing diet + alkalizing agents + intravenous vitamin C, the tumor in renal pelvis of the right kidney, which was found in January 2021, was significantly reduced in June 2021.*

*“Female, 76 years old, Malignant lymphoma of stomach, 2015/12, First visit to Wada Clinic. Her gastric malignant lymphoma disappeared two and a half years after her first visit to Wada Clinic, simply by changing her diet. All she did was to start an alkaline diet as alkalization therapy.” (Wada et al., 2022)*

## **Conclusion**

Escaping the acidic tumor microenvironment can be done. But it will take motivation, instruction, persistence, and professional guidance to pull it off. And, of course, nothing is certain. Could work. Could fail.

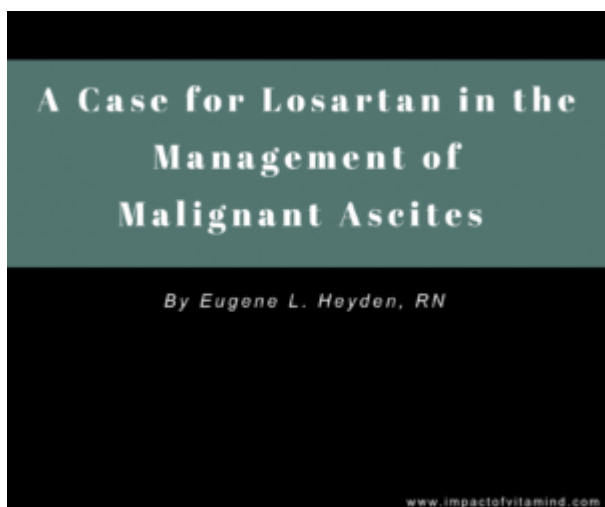
*“The biggest problem is that current medicine treats stage 4 cancer based on the assumption that it cannot be cured. To solve this problem, it is important to study people who have been cured of stage 4 cancer.” (Wada et al., 2022)*

## **Dedication**

To my beloved daughter Margaret



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