

Liposomal Vitamin C as a Vindication of an Old Idea

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Abstract

The fact that humans cannot synthesize ascorbic acid (vitamin C) from glucose leads to lower plasma levels of vitamin C and oxidative stress. The impact on immunity lies in increases in infection susceptibility, severity of organ failure, and mortality risk. Scurvy, a disease caused by vitamin C deficiency, has been known since ancient times. Regardless of the fact that people in developed countries have access to fresh fruits and vegetables, vitamin C deficiency is a serious problem worldwide. Traditional vitamin C supplements are convenient yet have very low bioavailability and can cause extreme stomach discomfort when consumed in large doses. The previous work of Ewan Cameron and Linus Pauling advocated high-dose vitamin C supplementation. Although this concept was initially embraced and then rejected, this article proposes that Cameron's and Pauling's ideas, like many mystical insights, were indeed ahead of their time. This paper challenges the traditional means of supplementation by arguing for the usage of liposomal vitamin C, a more bioavailable form of ascorbic acid, in both oral supplementation generally and intravenous delivery as a complementary clinical treatment of cancer and sepsis. For the time being, it may be considered a non-traditional method of supplementation, but that could change in the future. One day, we may refer to liposomal vitamin C as an adjunct to standard therapies or *the truth as we know it today*, especially if we keep an open mindset in the present.

La vitamine C liposomique, ou la confirmation d'une idée du passé.

par Lucie Kotlarova, PharmD

Résumé

Le fait que les êtres humains ne puissent pas synthétiser l'acide ascorbique (vitamine C) à partir du glucose conduit à des niveaux plus bas de vitamine C dans le plasma et au "stress oxydatif". L'impact sur l'immunité réside dans l'augmentation de la possibilité d'infection, dans l'augmentation de la possibilité de défaillance des organes et donc du risque de mortalité. Le scorbut, une maladie causée par une carence en vitamine C, est connu depuis l'Antiquité. Indépendamment du fait que les habitants des pays développés ont accès à des fruits et des légumes frais, la carence en vitamine C est un problème grave dans le monde entier. Les suppléments traditionnels de vitamine C sont pratiques, mais ils ont une très faible biodisponibilité et peuvent causer un inconfort gastrique extrême lorsqu'ils sont consommés à fortes doses. Les travaux d'Ewan Cameron et de Linus Pauling préconisaient une supplémentation en vitamine C à haute dose. Bien que ce concept ait d'abord été adopté, puis rejeté, cet article argumente que les idées de Cameron et Pauling, comme beaucoup d'idées mystiques, étaient en réalité en avance sur leur temps. Cet article remet aussi en question les

moyens traditionnels de supplémentation, en plaidant pour l'utilisation de la vitamine C liposomique, une forme plus biodisponible d'acide ascorbique, soit dans sa forme orale soit intraveineuse comme traitement clinique complémentaire contre le cancer et la septicémie. Pour l'instant, il peut être considéré comme une méthode non traditionnelle de supplémentation, mais ceci pourrait changer à l'avenir. Un jour, nous pourrions nous référer à la vitamine C liposomique comme à un complément thérapeutique standard, surtout si nous gardons un état d'esprit ouvert.

Vitamina C Liposómica como Reivindicación de una Idea Vieja

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Resumen

El hecho de que los humanos no puedan sintetizar ácido ascórbico (vitamina C) a partir de glucosa conduce a niveles plasmáticos más bajos de vitamina C y al estrés oxidativo. El impacto en la inmunidad radica en el aumento de la susceptibilidad a la infección, fallas severas de órganos y el riesgo de mortalidad. El escorbuto, una enfermedad causada por la deficiencia de vitamina C, se conoce desde la antigüedad. Independientemente del hecho que las personas en los países desarrollados tienen acceso a frutas y verduras frescas, la deficiencia de vitamina C es un problema grave en todo el mundo. Los suplementos tradicionales de vitamina C son convenientes pero tienen una biodisponibilidad muy baja y pueden causar molestias estomacales extremas cuando se consumen en grandes dosis. El trabajo previo de Ewan Cameron y Linus Pauling abogó por la administración de suplementos de vitamina C en dosis altas. Aunque este concepto fue inicialmente aceptado y luego rechazado, este artículo propone que las ideas de Cameron y Pauling, como muchas ideas místicas, se adelantaron a su tiempo. Este artículo desafía los medios tradicionales de suplementación al defender el uso de vitamina C liposomal, una forma más biodisponible de ácido ascórbico, tanto en la suplementación oral en general como en el suministro intravenoso como un tratamiento clínico complementario del cáncer y la sepsis. Por ahora, puede considerarse un método no tradicional de suplementación, pero eso podría cambiar en el futuro. Algún día, podremos referirnos a la vitamina C liposómica como un complemento de las terapias estándar o la verdad tal como la conocemos hoy, especialmente si mantenemos una mentalidad abierta en el presente.

Vitamina C Lipossômica como uma Reivindicação de uma Velha Idéia

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Sumário

O fato de os seres humanos não conseguirem sintetizar o ácido ascórbico (vitamina C) a partir da glicose, resulta em níveis mais baixos de vitamina C no plasma e em estresse oxidativo. O impacto na imunidade está no aumento da suscetibilidade à infecção, falha grave dos órgãos, e risco de mortalidade. O escorbuto, uma doença causada pela deficiência de vitamina C, é conhecida desde os tempos antigos. Independientemente do fato que as pessoas nos países desenvolvidos de terem acesso a frutas e vegetais frescos, a deficiência de vitamina C é um

problema sério em todo o mundo. Os suplementos tradicionais de vitamina C são convenientes, mas têm uma biodisponibilidade muito baixa e podem causar extremo desconforto estomacal quando consumidos em grandes doses. O trabalho anterior de Ewan Cameron e Linus Pauling defendia a suplementação em altas doses de vitamina C. Embora esse conceito tenha sido inicialmente adotado e depois rejeitado, este artigo propõe que as idéias de Cameron e Pauling, assim como muitas idéias místicas, eram realmente avançadas para aquela época. Este artigo desafia os meios tradicionais de suplementação, argumentando pelo uso da vitamina C lipossômica, uma forma mais biodisponível de ácido ascórbico, tanto na suplementação oral em geral quanto na administração intravenosa, como tratamento clínico complementar de câncer e sepsis. Por enquanto, pode ser considerado um método não tradicional de suplementação, mas que pode mudar no futuro. Um dia, poderemos nos referir à vitamina C lipossômica como um complemento às terapias padrão ou como a “única verdade” do conhecimento atual, especialmente se mantivermos uma mentalidade aberta no presente.

Liposomal Vitamin C , eine Verteidigung für eine alte Idee

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Zusammenfassung

Der Menschen kann aus Glukose keine Ascorbinsäure (Vitamin C) herstellen, was zu einem niedrigeren Plasmaspiegel und zu oxidativem Stress führt. Dies hat eine Auswirkung auf das Immunsystem wobei man anfälliger für Infektionen und ernsthafte Organfehler wird sowie das Sterberisiko erhöht wird. Skorbut, eine Krankheit verursacht durch Vitamin C Mangel, ist von jeher bekannt. Ungeachtet davon, dass die Menschen in den Industrieländer Zugang haben zu frischem Obst und Gemüse, bleibt dennoch das Vitamin C Defizit weltweit ein ernsthaftes Problem. Herkömmliche Vitamin C Präparate sind wohl dienlich, haben dennoch eine niedrige biologische Verfügbarkeit und können bei hohen Mengen extreme Magenprobleme verursachen. Die frühe Arbeit von Ewan Cameron und Linus Pauling empfahl ein hoch dosiertes Vitamin C als Nahrungsergänzung. Wengleich dieses Konzept anfänglich angenommen und später verworfen wurde, räumt dieser Beitrag ein, dass die Idee von Ewan Cameron und Linus Pauling, so wie es bei vielen mystischen Erkenntnisse der Fall ist, dennoch seine Zeit voraus war. Dieser Aufsatz fordert die traditionelle Bedeutung der Nahrungsergänzung heraus, indem Liposomal Vitamin C, eine mehr bioverfügbare Form der Ascorbinsäure, sowohl als gängige Tablette als auch in intravenöser Form, ergänzend bei der klinischen Behandlung gegen Krebs und Sepsis, verabreicht werden soll. Zurzeit wird dies als eine nicht traditionelle Methode der Ergänzung angesehen, jedoch könnte sich dies in Zukunft ändern. Eines Tages könnten wir das Liposomal Vitamin C als eine Ergänzung zu Standard Therapien, *oder die Wirklichkeit wie wir sie heute kennen*, sehen insbesondere wenn wir jetzt aufgeschlossen bleiben.

Introduction

Vitamin C (L-ascorbic acid) is a water-soluble micronutrient of interest for its effects on human health and its potential role in immune-related diseases. Yet, unlike other mammals, with the exception of guinea pigs and perhaps some species of bats, primates do not synthesize vitamin C in the liver and must therefore rely solely on dietary intake. Specifically, due to a mutation in the

gulonolactone oxidase gene (GULO enzyme is necessary for vitamin C production), humans cannot synthesize ascorbic acid from glucose. This leads to lower plasma levels of vitamin C and oxidative stress, unless counterbalanced with sufficient dietary intake from naturally vitamin C-rich foods, vitamin C-fortified foods, or supplements.

The rise, fall, and resurgence of high-dose intravenous (IV) pharmacologic ascorbate and oral ascorbic acid not only reminds us of Ewan Cameron and Linus Pauling's work in the 1970s, but illustrates how much in medicine is determined by *the truth as we know it today* and how easily innovative ideas can be rejected and then re-embraced.

The research work done by Linus Pauling, an American and originally a physicist, regarding high-dose Vitamin C supplementation was initially praised, especially since he had won the Nobel prize for Chemistry in 1954 for his work with molecules and their complex chemical bonds. He then turned from physical to biological chemistry and in 1970 published a popular book "*Vitamin C and the Common Cold*, in which he maintains that the common cold can be controlled almost entirely in the United States and some other countries within a few years through improvement of the nutrition of the people by an adequate intake of ascorbic acid."¹ Around the same time in Scotland, Ewan Cameron had been working on the idea that high dose vitamin C supplementation could benefit cancer patients by affecting a particular enzyme. He postulated "that the malignant invasiveness of cancer cells might be combated by manipulating hyaluronidase inhibitor, a naturally-occurring substance that controls the hyaluronidase enzyme liberated by malignant tumors."² Once aware of each other, both men began a long and productive collaboration. Unfortunately, their work was discredited under the assumption that oral high-dose vitamin C was not effective mainly due to inadequate clinical trials; Pauling in particular was assumed to be practicing a form of pseudoscience by testing megadose vitamin C on himself and then offering subjective results.

However, this paper proposes that vitamin C supplementation, when taken in liposomal form, can indeed be efficacious, not only for general health, but also as an adjunct to cancer and sepsis treatments, whether orally or intravenously administered in clinical settings. Pauling's work was ahead of its time, and like all mystics and visionaries whose initial ideas were not sufficiently recognized, we can posit that liposomal vitamin C supplementation is a vindication of Ewan Cameron and Linus Pauling's earlier vision. As a side note, Pauling can certainly be considered a mystic for his humanitarianism, anti-war stance, and nuclear-disarmament advocacy for which he received the Nobel Peace Prize in 1964.

History of Vitamin C and Scurvy

Although scurvy (scurbutus) was a known disease for centuries, ascorbic acid and its role in helping the body process carbohydrates, fats, and proteins was not discovered until the 1930s, isolated from plants in 1928 by Hungarian Dr. Albert Szent-Györgyi. Ascorbic acid soon obtained the name Vitamin C. Ascorbate is a mineralized version or salt of ascorbic acid, but these were unknown until the twentieth century.

To explain further, the history of scurvy is of note here. Known as early as 1550 BCE in Egypt, those deprived of vitamin C exhibited gum disease and other symptoms. "Hippocrates officially

termed the disease ‘*ileos ematitidis*’ with the description, ‘the mouth feels bad; the gums are detached from the teeth; blood runs from the nostrils... ulcerations on the legs; some of these heal... skin is thin.’³ The symptoms were also later described during the Middle Ages and the Crusades. We know that sailors of the past who lacked proper provisions, especially those on long voyages, developed symptoms of scurvy often leading to death. Further, in the late fifteenth century, the Portuguese explorer Vasco da Gama noted that citrus fruits alleviated symptoms on his voyages to India. However, little was known about the disease or what caused it.

It was during the eighteenth century that a Scottish naval surgeon, James Lind, through observation and testing noted that the symptoms of scurvy abated when citrus fruits like lemons and limes were given to sailors. Lind wrote that he made the discovery by separating the afflicted crewmen into groups fed the same diet, and he gradually introduced various foods. Those who received citrus improved while the others did not. Sadly, Lind and others later boiled lime juice for preservation on long voyages but did not know why it lost its efficacy, and his work also lost reputation. Vitamin C itself was not yet known nor the fact that high heat destroys it. Unfortunately, we consider scurvy a disease long buried in history since we assume that most people in developed countries consume a varied diet and thus should have no difficulty obtaining a sufficient daily supply of vitamin C. The availability of citrus fruits and other vitamin-C rich foods is widespread, yet vitamin C deficiency or depletion continues to be a serious problem worldwide. Many people today remain unaware that cooking or boiling fruits and vegetables high in this vitamin can reduce their quality, for example, berries, kale, broccoli, tomatoes, potatoes, and peppers. Also, some recent dietary trends, like the Keto diet that reduces carbohydrates in favor of fats, may have practitioners eliminate vitamin-C rich foods fearing they contain too much sugar, especially fruit. Smoking, alcohol consumption, pregnancy, and aging all increase risk for vitamin C depletion. Finally, in the absence of good health, hypovitaminosis C, occurring as a manifestation of prescorbutic (pre-scurvy) clinical outcomes, presents a significant concern.

Liposomal Vitamin C

Traditional vitamin C supplements are convenient, inexpensive, and readily available, yet have very low bioavailability and can cause extreme stomach discomfort when consumed in large doses. Some vitamin C-rich foods, like citrus, have similar drawbacks, and patients undergoing chemotherapy or with sepsis may find eating difficult in general. Low bioavailability is due to the transit through the digestive tract as the ascorbic acid encounters oral enzymes, digestive juices, and bile salts that essentially “use up” most of the antioxidant capacity.

Liposomal vitamin C differs from the over-the-counter products sold in most pharmacies. In liposomal C, the vitamin is encapsulated in liposomes (fats that are similar to those found in cell membranes) comprised of a phospholipid bilayer containing phosphatidylcholine.

Stomach upset is not the only reason to encapsulate vitamin C in liposomal form. There is a stronger pharmacokinetic reason (which examines the movement of substances through the body): after the oral usage of 1 g and more of ascorbate, there is just 200 mg of vitamin C absorbed because there are limited vitamin C receptors in the gastro-intestinal (GI) tract. The rest, if unabsorbed, is eliminated via the stool so that after a high oral intake of regular vitamin C, patients can experience diarrhea. This pharmacokinetic limitation is an important reason to

use the liposomal pharmaceutical form. In liposomal vitamin C, the spherical phospholipid structure provides absorption via membranes without the need of special receptors. Liposome encapsulated vitamin C is capable of reaching the liver non-oxidized and is 10 to 20 times more bioavailable than non-encapsulated vitamin C.⁴ Although more bioavailable than non-encapsulated vitamin C, liposome encapsulated vitamin C produces lower circulating concentrations than high-dose IV pharmacologic ascorbate administration.⁵ With a superior form of oral vitamin C available today, Cameron and Pauling's IV-oral vitamin C combination therapy is worth reconsidering.⁶

Vitamin C and Immune Function

Vitamin C impacts immune function by influencing multiple pathways including enhancing proliferation and differentiation of T-lymphocytes (T-cells) and B-lymphocytes (B-cells); stimulating natural killer (NK) cell activity; modulating cytokine production; acting as an antioxidant; and increasing collagen production in the fibroblasts.⁷ In otherwise healthy individuals, the immune system successfully prevents infections and random cancer cells from gaining a foothold and causing cellular havoc. Conversely, vitamin C deficiency leads to impaired immunity which increases infection susceptibility, severity of organ failure, and mortality risk. Proponents of vitamin C supplementation encourage its use to prevent and treat respiratory and systemic infections and to strengthen the skin as a barrier against pathogens. Prophylactic use requires dosing in the milligram range, whereas treatment of current infections requires dosing in the gram range. Metabolic demand and elevated inflammatory response necessitate higher dosages to combat the different stage of oxidative stress presented. Noteworthy is the fact that Ewan Cameron postulated that to have a sufficient effect on tumors and cancer cells, vitamin C delivery should be in the gram range.⁸

Vitamin C Deficiency in Cancer and Septic Shock Patients

Research suggests that cancer patients present with a higher incidence of vitamin C deficiency than patients with other diseases.⁹ Vitamin C deficiency has been observed in critically ill patients, as great as 75 percent, despite receiving the standard of care nutritional therapy.¹⁰ According to Carr et al., septic shock patients in the ICU experienced hypovitaminosis C at a rate of nearly 40 percent, compared to the non-septic, still critically ill patients, at a rate of 25 percent. The elevated inflammatory response accompanying septic shock is believed to induce severe vitamin C depletion; inflammation was measured by the pro-inflammatory biomarker C-reactive protein (CRP) and was higher in the septic shock patients. Carr's data also suggests that the ICU septic shock patients have scurvy by its definition (serum vitamin C level < 11.3 u/mol/l). Several clinical trials have begun investigating the use of intravenous vitamin C as an adjuvant in sepsis treatment.^{11,12}

Intravenous Ascorbic Acid in Cancer Treatment

Although cancer patients have low plasma levels of ascorbic acid, the treatment goal is not to correct the deficiency, but rather, a two-pronged approach to directly affect the cancer cells. First, Chen et al. showed that high-dose pharmacologic ascorbate induces oxidative stress in cancer cells without harming healthy cells;¹³ instead of the traditional idea of vitamin C

functioning as an antioxidant, at pharmacologic concentrations it functions as a prooxidant but only towards the cancer cells. The study observed sustained ascorbate radical and hydrogen peroxide formation within the interstitial fluids of tumors with a single dose in mice. Daily administration significantly reduced tumor growth rates for ovarian and pancreatic cancers as well as glioblastoma, a malignant brain tumor.

Second, Kuipers et al. rationalized utilizing high-dose pharmacologic ascorbate as a means to deliver sufficient ascorbate to the tumors to ensure optimal co-factor function, thereby halting tumor progression.¹⁴ Colorectal cancer patients whose tumors had a low ascorbate content, independent of grade and stage, did not survive in a disease-free post-surgery state as long as those patients whose tumors had higher ascorbate content.¹⁵ This suggests that the tumor's ascorbate content is the key factor in cancer survival.

Clinical data showed that high-dose IV pharmacologic ascorbate can be administered parallel with standard anti-tumor therapy to improve tolerance to chemotherapy, increase quality of life, and in some cases prolong time to relapse, reduce tumor volume, and prolong survival.¹⁶ Cieslak et al. in a review article¹⁷ examined use of high-dose IV pharmacologic ascorbate in treatment of pancreatic cancer and concluded that phase I trials have demonstrated safety and potential efficacy of ascorbate. Nauman et al. published in 2018 a systematic review of intravenous ascorbate treatment in cancer clinical trials.¹⁸ Single arm and randomized Phase I/II trials were included in this review. A total of 23 trials met the inclusion criteria. One trial¹⁹ was randomized: patients suffering from ovarian cancer were randomized to receive standard chemotherapy with or without intravenous vitamin C (IVC); that trial reported an 8.75 month increase in progression-free survival (PFS) and an improved trend in overall survival (OS) in the vitamin C treated arm. The authors of the review concluded that high-dose IV pharmacologic ascorbate has been shown to be safe in nearly all patient populations, alone and in combination with chemotherapy. Klimant et al. in another review published in 2018 summarized use of high-dose IV pharmacologic ascorbate in cancer care.²⁰ According to the authors, use of intravenous vitamin C is a safe supportive intervention to decrease inflammation in the patient and to improve symptoms related to antioxidant deficiency, disease processes, and side effects of standard cancer treatment. It can safely be used to treat ascorbate deficiency and could favourably affect clinical parameters such as inflammation, fatigue, and quality of life. Potential mechanisms of the action of high-dose pharmacologic ascorbate in cancer and clinical studies in this field were reviewed in another article published in 2018.²¹ The authors state that there is a substantial body of literature that documents potential anti-tumor effects of ascorbate in *in vitro* and *in vivo* settings, reporting cytotoxicity toward cancer cells and a slowing of tumor growth in animal models. Human clinical studies have suggested that high dose ascorbate treatment may have a clinical benefit for patients with pancreatic cancer and other advanced cancers. According to the authors, results of these studies have expanded knowledge of the biological functions of high-dose pharmacologic ascorbate, and, given its lack of toxicity, ready availability, and low cost, suggest there is a good rationale to use ascorbate as an adjunct treatment for cancer.

Ascorbic Acid Infusions: Limitations and Patient Burden

Despite the increasing use and promising efficacy of ascorbic acid infusion therapy in cancer patients, many unknowns, including dosing amount and frequency, timing of co-administration

with conventional chemotherapy, and treatment duration, exist and hinder the establishment of a standard of care.²² Studies suggest that the absolute minimum treatment includes 1 g/kg administered over two hours twice a week for at least two months; increased frequency (3x/wk) and longer duration (3-4 months or longer) are highly recommended.

Such recommendations involve financial, time, and convenience costs. This may place an undue burden on the patient and/or caregiver and in turn, cause patients to abandon type IV therapy protocols, especially if patients are paying out-of-pocket. Additionally, there may be no clinical trials offered within a patient's geographic area. Rather than discourage patients, it is perhaps time to consider a hybrid model of intravenous and oral ascorbic acid to complement chemotherapy and radiation.

Intravenous and oral ascorbic acid have also been included in the care of terminal cancer patients. Yeom et al. assessed health-related quality of life following a protocol of a 10 g infusion twice within a 3-day interval and 4 g orally every day for a week.²³ Patients reported improved physical, emotional, and cognitive function, and less fatigue, nausea, vomiting, pain, and appetite loss. Although these are subjective reports, this study suggests that despite mixed results and controversial research on vitamin C over the decades, therapeutic use of ascorbic acid is safe, and improving quality of life in terminal patients is not simply aspirational, but realistic. Currently, patients under the care of an integrative physician are more likely to receive any type of "natural" infusion therapy, and so, a physician's receptivity, or lack of, to nutritional intervention may be a limitation itself.

Liposomal Vitamin C: Beyond Cancer and Sepsis

Vitamin C status can be affected by various environmental conditions (i.e., air pollution, tobacco smoke), chronic diseases (i.e., diabetes, alcoholism), infections, and advancing age. These conditions are characterized by excessive and sustained inflammation in the body, which begs the question, *should daily oral liposomal vitamin C be included in the standard of care?* Vitamin C's immune-modulating effects suggest *yes*.

Furthermore, prophylactic use to prevent infections is advisable. Millions of people take vitamin C supplements or multi-vitamins with vitamin C every day, but the majority of these are of low quality and low bioavailability. A high quality, medically sourced liposomal form may be a little more expensive but provides the anticipated benefits. In other words, a little goes a long way, and stomach discomfort is not an issue. However as always, readers should use discernment when purchasing online since like many other supplements, there are also low-quality and fraudulent "liposome C" offerings. Regardless, true liposomal vitamin C presents a superior form of vitamin C delivery to the body.

Conclusion

Vitamin C therapy, whether administered intravenously or orally, is not without disagreement among cancer specialists. The one attribute that everyone can agree upon is the safety of liposomal vitamin C. Along with an obligation of "do no harm," it is also the medical community's duty to explore all potential options, even if that includes re-examining an old idea

with new eyes. Ewan Cameron and Linus Pauling’s exploration of vitamin C supplementation was visionary, and like all mystical insights that are not embraced in their time, deserves further research including more clinical trials and random controlled studies. For the time being, liposomal vitamin C may be considered an experimental means of improving health and well-being, what some might call a “bio-hack,” but that could change in the future and offer vindication for a promising idea. One day, we may refer to liposomal vitamin C as a complementary *standard-of-care* therapy or *the truth as we know it today*, especially if we keep an open mindset in the present.

Conflict of Interest

The author is Scientific Head of inPHARM CLINIC, Prague, The Czech Republic where liposomal vitamin C is administered as an adjunct treatment. This paper is meant to be purely informative and not intended to solicit financial or other benefits. She invites comments and questions at lucie.kotlarova@gmail.com

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Endnotes

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