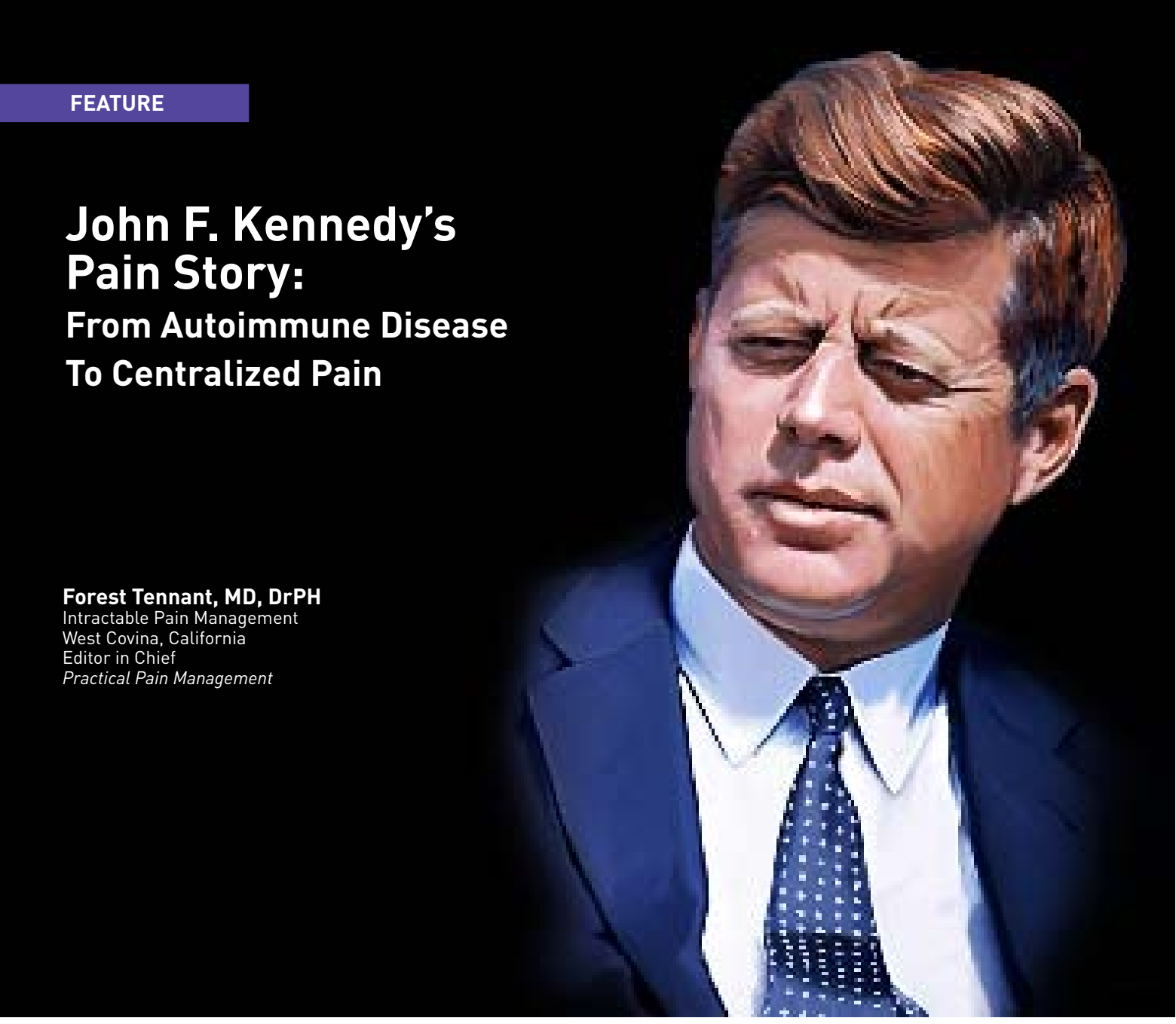
FEATURE

John F. Kennedy's Pain Story:
From Autoimmune Disease To Centralized Pain



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During John F. Kennedy's (JFK's) life, his medical condition was often shadowed in mystery. Although it was well known that JFK suffered from back pain, the true extent of his disability was a closely guarded secret. However, the release of his medical records in 2002, combined with advances in medical knowledge, has allowed researchers to unravel at least some of the mysteries of his case (see Box, see page 65).[1-8] In particular, since JFK's death in 1963, there have been three major advances in scientific understanding relevant to his condition:

- The life course of genetic autoimmune disease
- The development and impact of severe osteoporosis
- The development of centralized pain—a permanent imprinting of pain memory in brain cells

It is now believed that JFK suffered from a genetic autoimmune disease that emerged in early childhood and transformed into centralized intractable pain in adulthood.[4] A major motivation in presenting this report is to call attention to the growing importance of autoimmune diseases in pain practice. Autoimmunity may begin at birth with the production of autoantibodies; however, significant pain may not be present until adolescence or adulthood. Pain practitioners need to be fully appreciative of the lifetime course of genetic autoimmune diseases, and JFK's medical history provides a classic case from which to learn.

What Is an Autoimmune Disease?

In a normal immune system, antibodies circulate throughout the body and immediately attack and neutralize any infectious agent, poison, or toxic substance that may enter

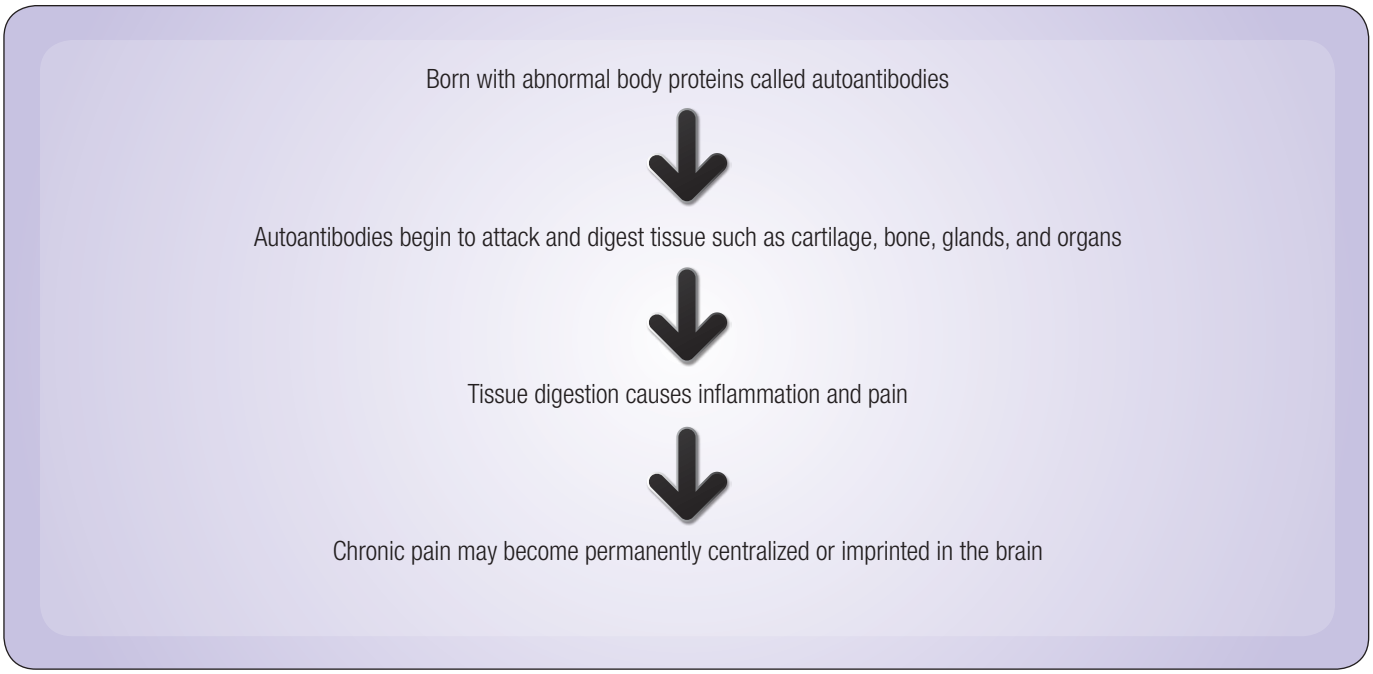

Figure 1. How a genetic autoimmune disease works.

the body. It is generally believed we all have some abnormal antibodies (autoantibodies) that are not life threatening, but give rise to problems such as mild vitiligo, psoriasis, or rheumatoid arthritis. Also, some physicians, including the author, believe that good health is dependent on keeping our autoantibodies in check by good health practices such as not smoking, exercise, and a balanced diet with nutritional supplements.

Autoimmune diseases, however, are caused by the presence of too many autoantibodies in the patient's blood that may be present at birth (Figure 1). Depending on the type of autoimmune disease, autoantibodies will attack cartilage, nerves, glands, bone, skin, lining of organs, blood cells, intestine, and even organs such as the liver, heart, or kidneys. In addition, having too many autoantibodies lowers a person's ability to fight off invading bacteria and viruses, making them prone to infections. Common early symptoms observed in childhood include fever, joint pain, rashes, nausea, headache, and diarrhea. These children may have many infections and are viewed as "sickly." Over time, the constant attack on the immune system causes inflammation and severe intractable pain.

In recent years, a growing number of patients with genetic autoimmune diseases have sought pain treatment for severe pain that developed in childhood and adulthood. This class of diseases includes such painful conditions as ankylosing spondylitis, Behçet's disease, Ehlers-Danlos syndrome, Marfan syndrome, and Schmidt's syndrome. Because these disorders are rare and often difficult to diagnose, patients may initially be given a vague diagnosis of myofascial pain, neuritis, or "muscle/ligament sprain," when in reality they have an undiagnosed genetic autoimmune disease. Table 1 lists some actual cases referred to my practice, which presented with just such a scenario.

The first realization that the body may attack its own cells came from studies of hemolytic anemia. Writing in 1955, William Dameshek, MD, stated that there may be "an extrinsic factor that can attack red cells in the circulation."[9] Interestingly, he uses the phrase "autoimmune process" as a rare possibility in the destruction of red blood cells. The first discovery that autoantibodies exist was published in 1956 when thyroid antibodies were discovered.[10] The concept of autoimmunity did not gain wide acceptance until the 1970s and '80s.[11,12]

The 1962 edition of *Dorland's Medical Dictionary* does not even list autoimmune disease.[13] The 1965 edition of *Current Therapy* only refers to "autoimmune reactions."[14] Slowly but surely the medical profession began to accept the fact that the body may actually turn on itself. In contrast to the 1962 edition, *Dorland's Medical Dictionary* in 1981 defined autoimmunity as "a condition characterized by a specific humoral or cell-mediated immune response against the constituents of the body's own tissues."[15] By 1989, *Taber's Medical Dictionary* succinctly defined autoimmune disease as we view it today: "Disease in which the body produces [a] disordered immunological response against itself.

Table 1. Clinical Pain-related Manifestations of Genetic Autoimmune Diseases[a]

Autoimmune Disease	Major Clinical Manifestations
Ankylosing spondylitis: inflammation of the joints in the back	Low back pain, arthritis
Behçet's disease: chronic inflammatory disorder	Inflammation of the joints, recurrent ulcers in the mouth, genitals; eye inflammation. Rare, chronic inflammatory disorder. May also cause various types of skin lesions, bowel inflammation, meningitis (brain and spinal cord), and cranial nerve palsies
Ehlers-Danlos syndrome: loose joints, hyperelastic skin, easily damaged blood vessels	Joint support structures; joint laxity, joint dislocation
Marfan syndrome: connective tissue disorder	Musculoskeletal manifestations include tall height, long arms and legs, flat feet, scoliosis or kyphosis; blood vessel disorder
Rheumatoid arthritis: inflammation of the joints and surrounding tissues	Joint stiffness and pain, loss of range of motion
Schmidt's syndrome: autoimmune polyglandular syndrome type II	Addison's disease (adrenal insufficiency), thyroid disease, diabetes, and/or gonadal failure
Still's disease: juvenile rheumatoid arthritis	Joint stiffness and pain, loss of range of motion
Systemic lupus erythematosus	Skin rash, generalized pain, inflammation of tissue linings and coverings

[a]All these genetic immune diseases have multiple clinical manifestations, which may overlap each other. These diseases emerge in childhood, but a patient may not develop severe pain until adulthood. Some are not diagnosed until adulthood. This is not a complete list.

Normally, the body's immune mechanisms are able to distinguish clearly between what is a normal substance and what is foreign. In autoimmune diseases, this system becomes defective and produces antibodies against normal parts of the body to such an extent as to cause tissue injury."[16]

JFK's Genetic Autoimmune Disease

A common misconception is that JFK's back and pain problem began when the patrol torpedo (PT) boat 109 was demolished by a Japanese destroyer in World War II. Indeed, his back pain was worsened by the accident requiring an operation in 1944, but his pain problem began long before this mishap (see Timeline, page 56).

Following the release of JFK's medical records, there was much speculation about what caused his medical problems. In 2009, Lee Mandel, MD, a Navy physician, astutely analyzed JFK's medical history for clues—from childhood through his presidency—and came to the conclusion that JFK most likely had autoimmune polyglandular syndrome type II, also known as Schmidt's syndrome (Table 2, page 60).[4] Dr. Schmidt was a German pathologist who in 1926 described two cases of persons who died from adrenal failure and thyroiditis.[17] Over the years this genetic autoimmune disease has been well described.[18-22]

The first clue to Dr. Mandel's "diagnosis" was the fact that JFK was a "sickly" child. According to family records, his autoimmune disease began to exhibit itself in the first two years of life—when he suffered from almost constant infections during infancy, including scarlet fever. His symptoms continued throughout childhood and included nausea, diarrhea, joint pain, headache, fever/infections, and fatigue. As he approached adolescence, JFK's main symptoms included diarrhea/nausea and weight loss, which required multiple hospitalizations. At the Mayo Clinic he was diagnosed with colitis, but today it would likely have been called celiac disease, which is a common component in the autoimmune polyglandular syndrome and other genetic autoimmune diseases.[4,23,24]

In the late 1930s, some of JFK's physicians were astute enough to try the newly developed corticosteroid desoxycorticosterone acetate (DOCA) to help manage his colitis. This was the first time physicians could administer a cortisone derivative (in the form of pellets implanted under the skin) and JFK responded. His nausea and diarrhea improved with DOCA, and the treatment allowed him to proceed with college. While this bold move by his physicians probably saved his life,

DOCA may have caused an unexpected consequence—osteoporosis.[1]

The Pain Begins

By the age of 15, JFK had aches in various parts of his body and had severe pain in his knees. Over the next two years he lost weight, had fevers, and developed hives. Although not diagnosed at the time, today these presenting symptoms may have caused doctors to diagnose JFK with juvenile rheumatoid arthritis or Still's disease.

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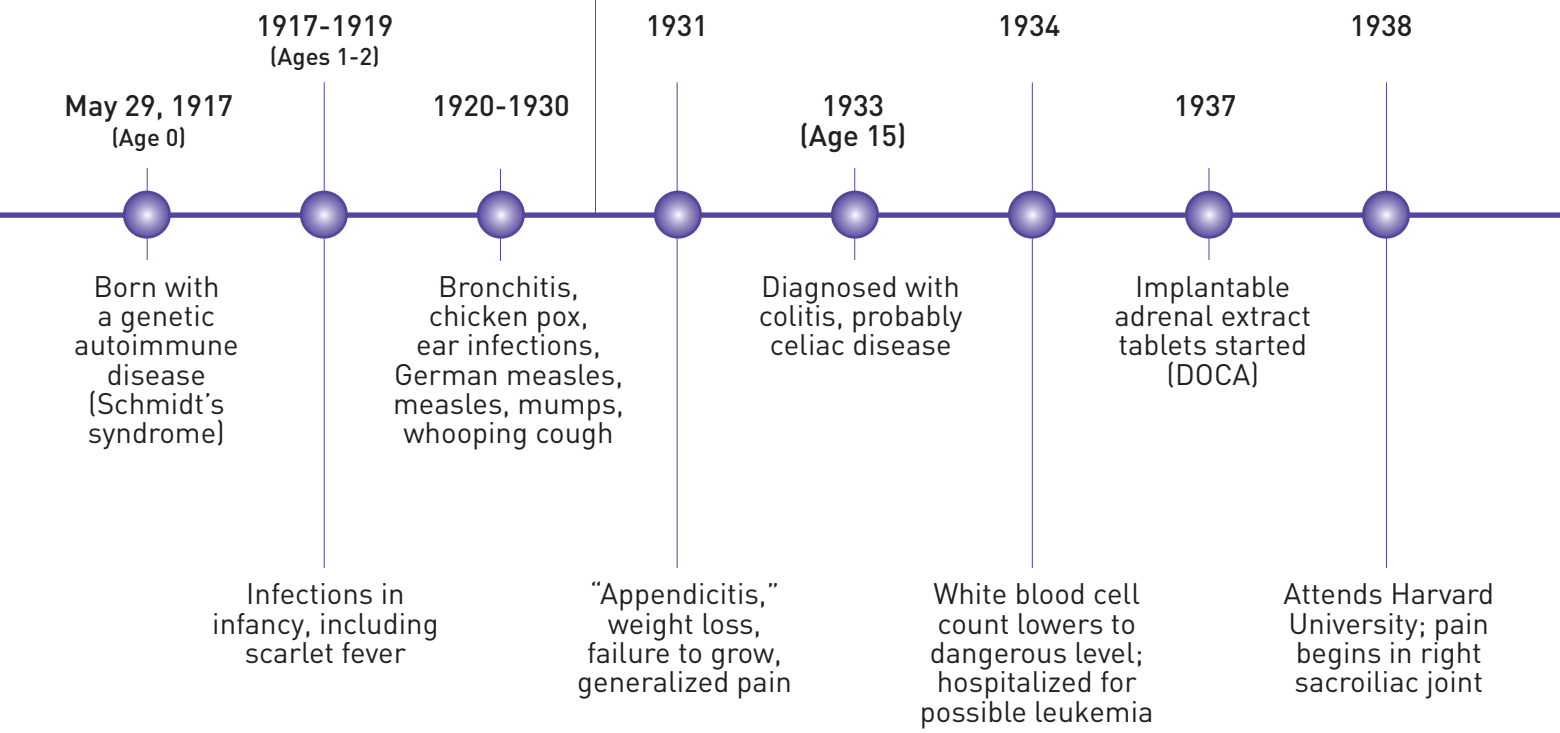
John F. Kennedy, as a teenager, working on a sailboat looking gaunt.

By the age of 21 (1938), an ominous symptom began to appear—JFK began having occasional pain in his right sacroiliac joint. Although the pain would disappear, it kept returning and was a little worse each time. Because there was no recorded precipitating injury or fall, it can be surmised that this first pain site meant that his autoimmune genetic disease was attacking the cartilage and lining of this joint. About two years later in 1940 while playing tennis, JFK experienced a sudden pain in his lower right back and he remarked that "something had slipped." He was hospitalized for 10 days at the Lahey Clinic, where he was fitted for the first of many back supports that he would wear the rest of his life. His back pain slowly progressed, but it didn't stop JFK from enlisting in the Navy and being assigned to a PT boat in the South Pacific. To enter the Navy he had to use his father's influence and likely withheld medical information from his military doctors.

While in the Navy, JFK's back problems were recorded by Lennie Thom, JFK's executive officer. He wrote letters home discussing JFK's back problems and his refusal to report to sick bay. "*Jack feigned being well. Kennedy did not let on to his crew or his commanding officer that he was ill or in pain. He couldn't, however, hide his chronic back ailment since he always wore a corset-type brace and kept a plywood board under his mattress.*"[1]

Undoubtedly the sinking of PT 109 and JFK's three-mile swim to rescue didn't help his ongoing degenerative spinal condition. The nature of autoimmune degeneration is one that seems to wax and wane—everything is fine for a while, but then symptoms return. Indeed, both



JFK's intestinal and back problems resurfaced before the war ended. In 1944, JFK underwent the first of two major back surgeries. According to Naval records, "during back surgery some soft disc interspace material was removed."[1] Navy medical records also indicate that there was clear evidence osteoporosis was present at surgery.[1] Unfortunately, little was known about the cause, treatment, and prevention of osteoporosis in 1944.

The Great Disabler: Osteoporosis

Although the cause of JFK's early osteoporosis cannot precisely be determined, it was likely precipitated by more than one factor. There are three possible reasons why JFK developed osteoporosis at such a young age. First, JFK's autoimmune disease undoubtedly attacked his bones.[25,26] It has been recognized that adrenal insufficiency (Addison's disease, which is a component of Schmidt's syndrome) is associated with osteoporosis.[26] Second, severe pain, per se, may cause cortisol from the adrenal gland to be excessively secreted into the blood stream. Initially, the body is flooded with hormones, but if the stress response persists over a long period of time, the body's organs become depleted of hormones. Any mechanism that causes excess serum levels of cortisol can produce osteoporosis.[27] By 1944, when osteoporosis was diagnosed, JFK had suffered bouts of back and abdominal pain for at least 6 years, which is enough time for severe chronic pain to produce osteoporosis. The third mechanism, as noted by Dallek, was the administration of DOCA.[1] It is unknown how often JFK may have used these implanted pellets—each implant lasted about 3 months—but dosage and effect on serum cortisol were unknown at the time. Today, we know that implanted medication in tablet form tends to produce excess

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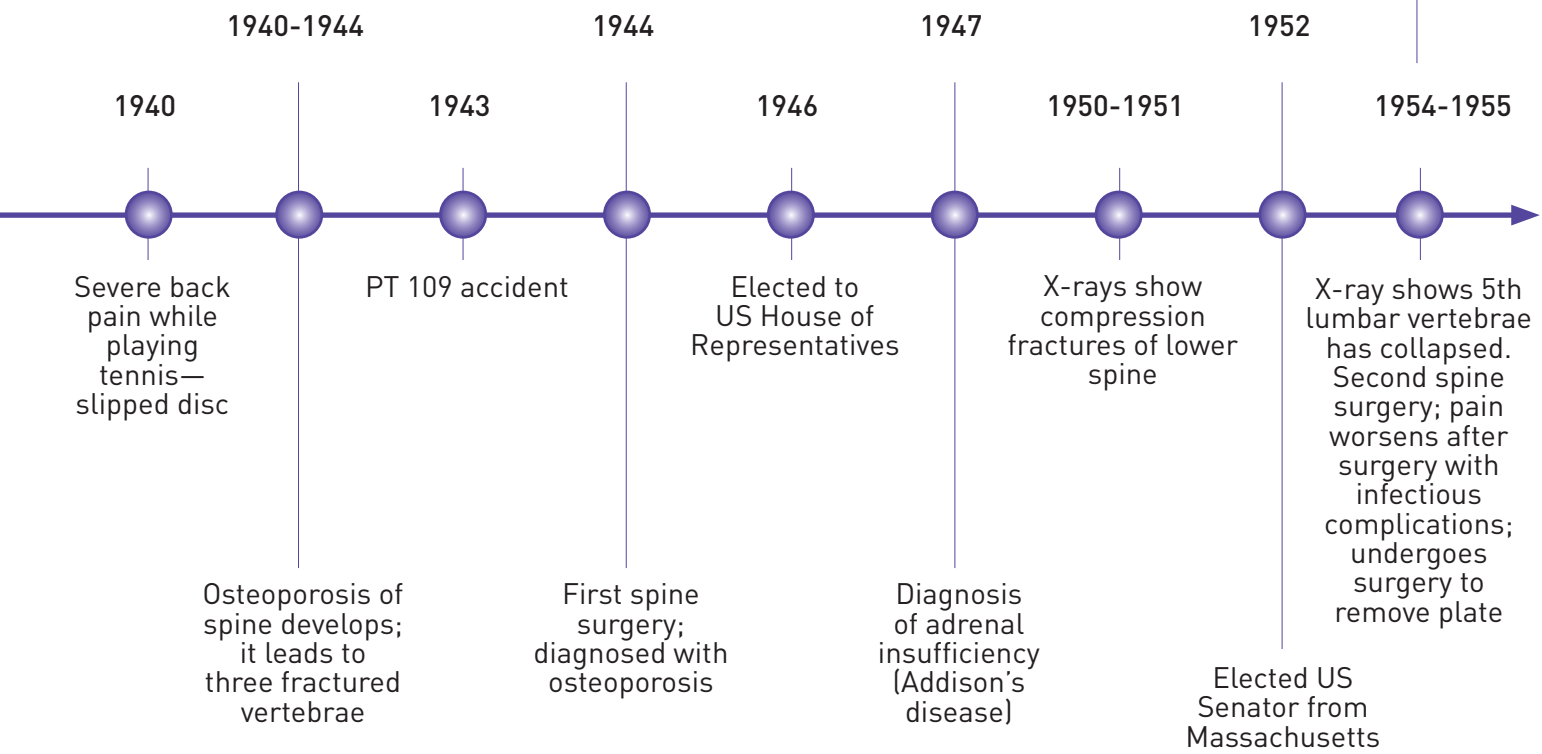
Senator John F. Kennedy, on crutches, and Jacqueline Kennedy enter the Hospital for Special Surgery in New York to undergo his second back surgery.



DOCA, desoxycorticosterone acetate; PT, patrol torpedo

TIMELINE CONTINUED

blood levels at times, and too little at others. Because there are no blood tests recorded at the time, we will never know exactly what caused his osteoporosis—insufficient cortisol caused by his autoimmune disease or a combination of pain-induced release of cortisol combined with the administration of exogenous steroids.

What is known is that JFK's osteoporosis continued to progress. In 1947, while traveling in England, JFK was officially diagnosed with Addison's disease. In 1950 and 1951, x-rays showed narrowing of the fourth lumbar vertebrae and some compression fractures. By 1954, when JFK was the junior senator from Massachusetts, his fifth lumbar vertebrae had collapsed. He was in such severe constant pain that he required crutches. Despite the risk of performing an operation in someone with adrenal insufficiency, JFK decided that the choice between walking and not walking was worth the risk. On October 21, 1954, at the New York Hospital for Special Surgery, he had his second major back surgery. A metal plate was inserted to stabilize his lower spine. Within 3 months, however, the plate became infected and so in February 1955, it had to be removed. His mother, Rose Kennedy, said later, "Jack was determined to have the operation. He told his father that even if the risks were fifty-fifty, he would rather be dead than spend the rest of his life hobbling on crutches and paralyzed by pain."[1]

By the time of his second back surgery in 1954, his pain had

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JFK, meeting Dr. William Menninger, in his famous rocking chair in the Oval Office.

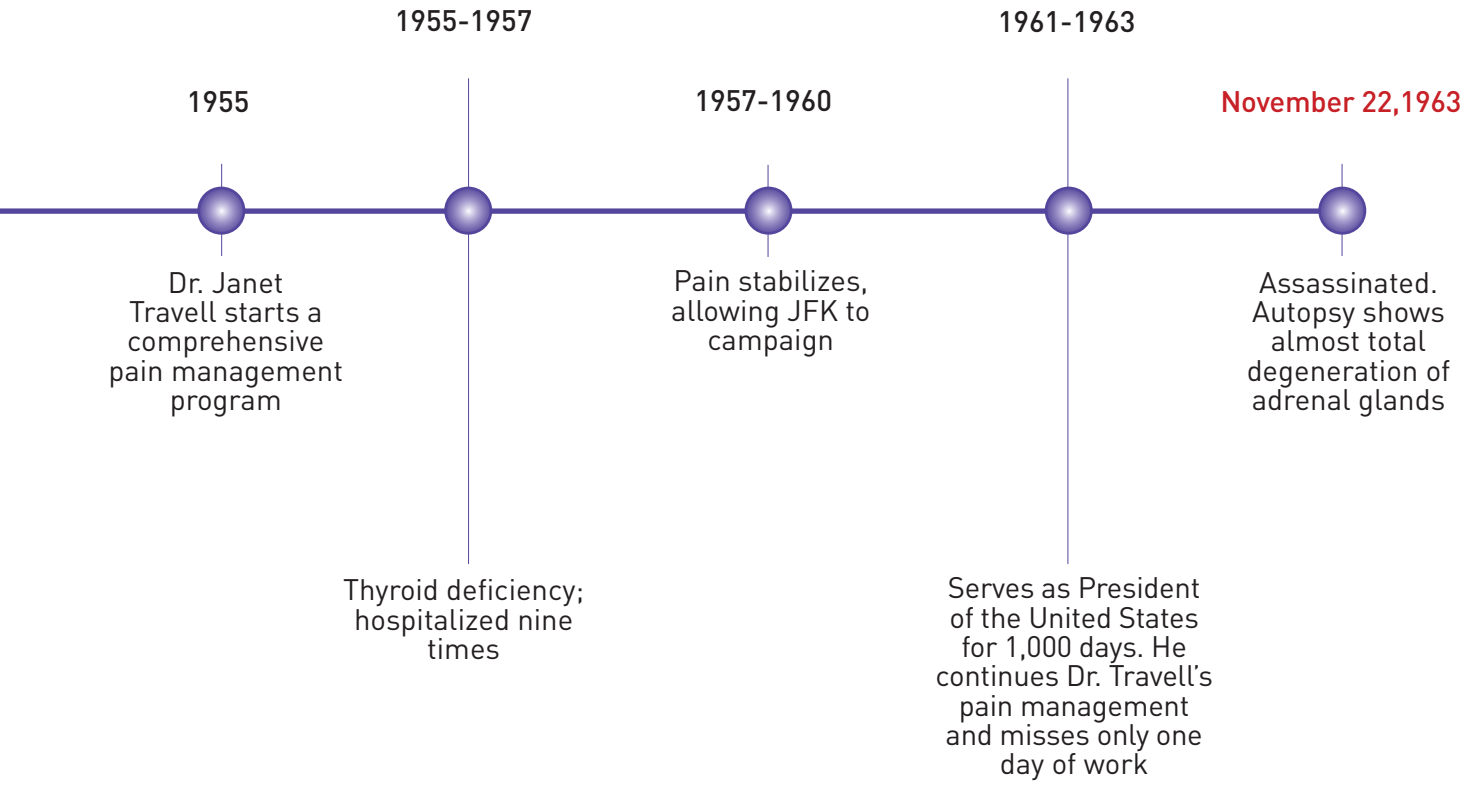

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Table 2. Characteristics of JFK's Genetic Autoimmune Disease	
Assigned name[a]	Schmidt's syndrome or autoimmune polyglandular syndrome type II
Major clinical manifestation	Adrenal and thyroid degeneration
Secondary clinical manifestations	• Celiac disease/colitis/irritable bowel syndrome • Anemia • Degeneration of cartilage, discs, bone with pain • Osteoporosis
Supporting laboratory evidence	• Agranulocytosis (low white count) • Adrenal glands almost absent at autopsy
Heritage	Sister Eunice had Addison's disease; son, John F. Kennedy, Jr., had Graves' disease

[a]Genetic autoimmune diseases have a given name usually based on the person who first described the disease. Although each genetic autoimmune disease has major clinical manifestations, the autoantibodies circulate in the blood and may attack different tissues giving a varied clinical picture.

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undoubtedly centralized, meaning that he didn't just have an inflamed, spastic, painful back—rather, the pain had imprinted itself in the cells of his brain (Table 3).[28-30]

JFK Meets Dr. Janet Travell

In 1955, JFK was at the lowest point in his health—his genetic autoimmune disease had wiped out considerable adrenal function, he had suffered numerous infections and muscle spasms, and was in constant pain. Despite the promise of surgery, he could not turn his body or walk without crutches. Fortunately, his endocrinologist, Ephraim Shorr, MD, was well acquainted with Janet Travell, MD, who, along with her physician father, had been studying back pain and muscle spasm for many years.[31,32] At the time Dr. Travell was probably the best pain specialist in the world.

Dr. Shorr arranged for JFK to meet Dr. Travell at her office in New York City on May 26, 1955. This was JFK's lucky day. On first meeting JFK, Dr. Travell describes Kennedy's plight in her autobiography[6]: *"Senator Kennedy seemed tired and discouraged. He listened intently, but he answered my questions briefly, almost reluctantly, as if he were retelling a boring story. He looked thin; his weight of about 155 pounds did not adequately cover his generous frame and stature of six feet. In spite of his Florida suntan, I thought that he appeared pale and anemic, and that indeed proved to be the case. He moved guardedly. He turned his body in one piece when he wanted to face me or Dr. Shorr; Eph and I sat on opposite sides of a wide desk, while his chair was placed at one end. Not only the motion of his back, but also the rotation of his neck was restricted. When I examined him, the reality of his ordeal was brought home to me by the callus under each armpit toward the shoulder blade where the skin had borne his weight on crutches for so long."*

On first meeting Dr. Travell, JFK wasn't very impressed. Like most intractable pain patients I've ever seen, they have gone to scores of doctors who want to perform another surgery, nerve block, or prescribe some worthless

Table 3. How Centralized Pain Develops: A 4-step Process

1. A painful injury to peripheral nerves occurs
2. The injury doesn't heal within a few weeks, so inflammation particles from the pain site migrate into the spinal cord and brain
3. Cells called "glia" activate and form inflammatory sites in the brain
4. The inflamed sites trap and imprint the memory of pain so it is constantly present

Common Characteristics of Centralized Pain

- Pain doesn't completely resolve
- Pain becomes constant
- Surgery doesn't help
- Severe insomnia
- Pain comes in waves with episodes of spasm
- Cold hands and feet
- High blood pressure and elevated pulse rate

Table 4. Dr. Travell's Pain Treatment of JFK	
Physical exercises	Rocking chair Swimming Muscle stretching/strengthening
Medications	
Opioids	Methadone (Dolophine), meperidine (Demerol), codeine
Bedtime sedative/sleeping aid	Barbiturates (Tuinal)
Muscle relaxants/anxiety	Meprobamate (Miltown), chlordiazepoxide (Librium)
Topical/local anesthesia	Procaine injections
Stimulant[a]	Methylphenidate (Ritalin)
Hormones	Oral hydrocortisone, DOCA implants, prednisone, methyltestosterone, liothyronine
Infection control	Gamma globulin
Vitamins	B_{12}, B, B-complex
Physical measures	Heel lift Back brace and corset Special chairs

[a]JFK may have received additional stimulants and what is believed to be human chorionic gonadotropin injections from a private physician outside the White House.
DOCA, desoxycorticosterone acetate

non–pain-relieving medication. Dr. Travell laments his discouragement. "*He asked a few questions, always to the point. How long would the improvement in the motion of his knee last? He was understandably skeptical. He was not prepared to accept readily one more doctor and another kind of treatment. Seven months earlier he had undergone a lumbar spine fusion, after which a plate had been removed in a second operation. His crutches had been a familiar sight in the Senate during the summer of a year ago, and now he was still obliged to use them.*"

However, Dr. Travell wasn't dismayed by JFK's skepticism. After all, he had come to see Dr. Travell because of what she called his "stubborn hope for better health and respite from pain." After consultation with Dr. Shorr, Dr. Travell felt JFK should immediately enter the hospital to begin medical treatment. Unlike today, in 1955 it was routine to admit a patient to initiate treatment. She started JFK on a comprehensive medication, rehabilitation, and exercise program that saved his life, gave him hope, and gave him the pain relief he needed to serve as a senator and later become president of the United States. Since Dr. Travell's time, those of us who have followed in her footsteps have a standard treatment goal for severe pain patients like JFK: pain relief, normal physical and mental function, and a quality of life!

Dr. Travell's Pain Treatment

While in the hospital, Dr. Travell began JFK on a pain treatment regimen that is a marvel by even today's standards. Her precise regimen remained a mystery until JFK's medical records were opened. Although his medical records have been analyzed, criticized, and even condemned by various parties, to a pain specialist like myself who treats centralized intractable pain, they reveal a truly amazing and incredible treatment regimen. What are unknown, unfortunately, are the precise dosages, titration schedules, and timing of how she used JFK's medications.

Dr. Travell's treatment was a comprehensive approach that included analgesics, physical measures, hormone replacement, and attempts to slow down his autoimmune disease (Table 4). Medical records kept by Dr. Travell over the course of her 8-year treatment reveal that JFK was prescribed the following medications: codeine, meperidine, methadone, methylphenidate, meprobamate, barbiturates, liothyronine, gamma globulin, cortisone, testosterone, and procaine injections.[1-4]

Within about 3 months after starting Dr. Travell's treatment regimen, JFK's pain was immensely better and he was

back to work as a senator from Massachusetts and planning his run for the presidency. So grateful was JFK and his wife that they invited Dr. Travell to visit with them in Palm Beach late in 1955. To emphasize the effectiveness of her treatment, I quote from her autobiography: "I had no idea that before the year (1955) was out I would sit at the table in Palm Beach, where he wrote '*Profiles in Courage,*' in the company of a revitalized John F. Kennedy." Even more telling that his pain was controlled is the fact that he took dozens of campaign trips between 1955 and 1960. What's more, he served 1,000 days as president and only missed one day of work. Any pain management specialist today would be proud of this result in such a tragic case.

The 1950 Standards For Pain Treatment

When Dr. Travell's treatment, and particularly the list of medications, were initially revealed in 2002, there was great angst as many of JFK's medications are potentially abusable.[3] Despite some controversy, his treatment regimen was, in actuality, the forerunner of today's treatment for intractable centralized pain.[3] His medication list is quite similar to the one used today. It's the "last stand" when all else has failed. Dr. Travell knew how to safely and effectively prescribe medications. She was an "old pro." It is also cogent to point out that JFK's treatment program was not particularly controversial when Dr. Travell initiated it in 1955.

For example, the 1956 *Merck Manual*[33] stated relative to pain treatment: *"More severe pain requires the oral or subcutaneous use of codeine, meperidine, methadone, dihydromorphone, metapon, or morphine. The effectiveness of these analgesics often may be enhanced by judicious use of antispasmatics or mild sedatives."*

The 1955 *Physician's Desk Reference* categorized pain analgesics for use in cancer, labor, muscular, neuralgic, postoperative, and postpartum conditions.[34] Kennedy's condition would fall under muscular, neuralgic, and postoperative. Methadone (Dolophine), as well as meperidine (Demerol) and procaine injections were listed under muscular and neuralgic conditions. In summary, Dr. Travell's medications were standard of the day.

Opioids

In the hands of a very experienced pain specialist, methadone, meperidine, and codeine can be excellent, long-term pain treatments. JFK was a clear benefactor. Methadone is a long-acting opioid that provides great stability to a centralized pain patient. It can provide the kind of pain suppression and mental and physical stability to someone who has a demanding schedule. Meperidine is an excellent fast-acting short-duration opioid that can extinguish pain flares or what is now called "breakthrough" pain. In my experience, codeine (Fioricet) works particularly well on certain types of pain.

One thing, however, is very clear to this author. In May 1955, JFK was "down for the count" and "gravesite ready" due to severe centralized intractable pain. When Dr. Travell took charge, the only hope to save him, given her therapeutic options, were methadone and meperidine.[33,34]

Unless the physician truly has an understanding and expertise in prescribing these opioids, particularly methadone, they are dangerous. In recent years inexperienced physicians have tried to prescribe methadone and are now responsible for an epidemic of overdoses.[35] The synthetic opioid has a negative reputation in the minds of some persons because it is used to detoxify or maintain heroin addicts. This is unfortunate because first-class pain specialists often get first-class results with it just as Dr. Travell did with JFK.

Muscle Relaxants and Sedatives

Centralized pain has a characteristic that disables patients. Normally, the central nervous system (CNS) tightly controls the outflow of electricity from the brain to the muscles. When pain becomes imprinted in the brain and causes CNS inflammation, the usual electrical control is lost or markedly reduced.[30] This loss of control results in too much electricity flowing from the brain to the peripheral tissues. This condition is marked by waves of pain sometimes called allodynia. The wave can cause bizarre feelings like worms or spiders crawling on the skin or intense burning or itching. Mainly, however, the uncontrolled electricity causes muscle spasms that feel like being shaken on a vibrator, causing severe anxiety. JFK received meprobamate (Miltown) and chlordiazepoxide (Librium), which are excellent drugs for this situation. Other symptoms related to the excess electrical discharge include hypertension, increased heart rate, nausea, and blood vessel constriction, the latter of which gives the patient a sensation of cold hands and feet.

Insomnia

Constant pain and the excess electrical discharges keep the centralized pain patient awake. JFK had to take barbiturates (Tuinal) to get some sleep, and almost all centralized pain patients require a potent sleep aid.

Stimulants

Many severe centralized pain patients can't get adequate pain relief without use of a stimulant. In the late 1800s, physicians at the Brompton Hospital in London recognized that substantive pain control required the simultaneous administration of an opioid and a

stimulant. JFK was prescribed methylphenidate (Ritalin), which is still widely used today in centralized pain patients. Although it is widely recognized that stimulants, either amphetamine or a derivative, provide considerable pain relief in centralized pain patients, their mechanism of action is unclear. It is generally believed that these compounds enhance endogenous stimulant neurotransmitters such as dopamine and noradrenaline in the CNS.[36]

Testosterone

Kennedy was prescribed testosterone, starting with oral methyltestosterone 10 mg/d and increased to 25 mg/d during periods of stress. By 1962, his physicians began trying different testosterone preparations—testosterone aqueous suspensions (50-75 mg) and oral fluoxymesterone (5-10 mg/d).[4] The reported reason was to keep up his weight. Although unknown to physicians in JFK's era, testosterone is a critical hormone for pain management in males and females. Severe pain as well as the opioid drugs taken by JFK lower testosterone blood levels and replacement must be given. Testosterone is not only anabolic and builds muscle and other tissues, but it has a direct CNS pain-relieving effect. JFK fathered four children under Dr. Travell's care, so there is little evidence that his sexual abilities were impaired by his pain problem or medications. Today, clinicians no longer prescribe oral testosterone formulations—instead, testosterone is prescribed as injections, gels, and patches, which have been shown to be more effective.

Procaine

Dr. Travell was clearly an expert in the use of injectable procaine.[32] She would inject the president up to 2 to 3 times per day if he was having a severe pain flare. The 1955, the *Physician's Desk Reference* said this about procaine[34]:

"*Procaine hydrochloride, one of the oldest drugs in current use, continues to be the local anesthetic of choice for many infiltration and other anesthetic procedures. Recently it has also been used with a high degree of success as an analgesic and therapeutic agent. Procaine has proved effective in relieving arthritic symptoms, controlling postoperative pain, easing edema, and pain of trauma.*"

Today, procaine has been replaced by other caine anesthetics so that physicians can choose between patches, ointments, or infiltration. The caine anesthetics are, as they were in the time of JFK, essential for pain practice.

Vitamins

Dr. Travell believed JFK had a peripheral neuritis caused by vitamin B deficiencies when she first examined him in 1955.[6] Her basis was loss of vibratory sensation in his legs. She prescribed vitamin B and B_{12}. Modern-day pain specialists are also big on B vitamins. For example, I recommend all my intractable centralized pain patients take extra B_{12} each week on top of a daily vitamin/mineral preparation and fish oil.

Thyroid

All genetic autoimmune diseases are progressive to at least some degree. JFK's autoimmune polyglandular syndrome first affected his adrenal glands but eventually attacked his thyroid gland. Dr. Travell had to start him on thyroid replacement in 1955 (liothyronine) and he took it continuously until death. If JFK had lived longer, other glands such as the pancreas or pituitary may have been affected.

Cortisone

JFK's denial of Addison's disease and the attendant controversies and publicity around this issue have obscured the key role that cortisone or lack of it played in JFK's pain problem.[1,3,5] A basic fact is that real cortisone for oral use was not developed until 1950. Prior to this time only adrenal extract in the form of implanted pellets were available (DOCA). Unfortunately, the precise dosage of these implanted tablets was always uncertain, and unlike today, there were no reliable, rapid blood tests to determine whether too little or too much cortisone was being given. JFK may have received too little or too much at different times over the approximate 25 years he took cortisone derivatives, but proof is conjectural. At only one period in the late '50s did he show the classic sign of a rounded face known as a "moon face," which suggests excess cortisol.

One of the major criticisms ascribed to JFK's cortisone use is that he should never have taken it because it may have caused osteoporosis and degeneration of his adrenal glands.[1] This criticism, I believe, is grossly wrong. The invention of DOCA in the 1930s was a marvelous advance. It undoubtedly saved many people's lives including JFK's. It is highly possible that JFK would never have seen a PT boat if it weren't for DOCA. His intestinal problems and pain responded to DOCA although it may have contributed to his osteoporosis and adrenal degeneration. How often JFK used the pellets is unknown but he undoubtedly used them for flares of his colitis and pain. A friend of JFK, Paul Fay, saw him implant a pellet. He described it this way[1]:

"*By using a little knife, he just barely cut the surface of the skin, tried not to get blood, and then get underneath and put the tablet underneath the skin, and then put a bandage over it.*"

Pure cortisone derivatives were not developed until 1950, and JFK's physicians skillfully maintained him on these until death. The simple fact is that JFK's adrenal glands failed in the mid-1940s and he required daily cortisone

thereafter to maintain life. Today, we know that good pain control of severe centralized pain can't be done in any patient unless the body maintains a good level of cortisone.

Rocking and Swimming

I've taken the liberty to group Dr. Travell's instructions on use of a rocking chair and swimming together because I consider both to have critical, basic physiologic effects on pain patients. In my clinic these effects are known as the "electricity and lymph flow" exercises. My personal theory stems from the fundamental fact that pain at its most basic form is an accumulation of too much electricity and inflammation at one site in the body. In 1791, Dr. Luigi Galvani, a physician for whom the galvanometer is named, performed many experiments on deceased persons and frogs.[37] He discovered that electricity collects around damaged nerves, and he coined the term "current of injury." Since pain patients such as JFK have many damaged nerves and have loads of inflammation, they must daily take measures to remove the electricity and inflammation from the pain site lest matters worsen. One of the problems with centralized pain is that the brain keeps sending electricity back to the original pain site.[28,30]

In the author's opinion, there's no better way to move electricity and inflammation out of a pain site than rocking and swimming. While electricity primarily moves along intact nerves, which are really wires, inflammation must be carried away from a pain site by the lymphatic system. This is a system of very small channels between cells that exist to carry away toxins and the dead tissue of inflammation. Excess body electricity must make its way to the skin surface via very small nerve endings so it can escape into the air.

Although Dr. Travell doesn't recite any theoretical claim as to how a rocking chair or a swim can help pain patients, she knew they worked and knew that these were essential components of her treatment program.

Although Dr. Travell doesn't recite any theoretical claim as to how a rocking chair or a swim can help pain patients, she knew they worked and knew that these were essential components of her treatment program. On the day she first met and hospitalized JFK in May 24, 1955, she took an old-style North Carolina porch rocker to his hospital room much to the amazement of the floor nurses. She colorfully described the incident[6]:

"*I parked my car at the delivery entrance to the hospital and transported the rocking chair up in the freight elevator. The nurses thought it funny to see the chair coming down the hall with the loose rockers, a leather cushion, a sloped footstool, and my medical bag on top, all stacked on the chair seat.*"

Since that day, Dr. Travell made sure that hardly a day went by without JFK doing a little rocking. She also highly encouraged him to swim. In late 1955, at the Kennedy home in Palm Beach, she told JFK he was now strong enough to swim in the ocean. Dr. Travell believed that salt water and the lift and fall of ocean swells were a "rocking horse sea."[6] She actually accompanied JFK on his first ocean swim after his surgery. As president, he swam in the White House pool almost daily.

Most pain practitioners today use a variety of measures that mimic what a rocking chair or swim can do. The idea is to keep lymph draining and excess electricity moving to reduce pain and promote healing. Included in these measures are massage, vibration, trampoline, walking, aquatic exercises, copper bracelets, and magnets.

Physical Rehabilitation

Dr. Travell was a marvel at physical rehabilitation measures. She had a keen interest in how shoes, chairs, and braces put stress on back muscles.[31] She found that JFK had a left leg about an inch shorter than his right. As a result she made him a heel lift to keep him balanced. She designed special chairs with a writing table attached so he could sit and write without back strain. JFK used a variety of back braces and corsets, which Dr. Travell designed.

Besides procaine injections when his back pain flared, Dr. Travell and the other White House physicians used ultrasound and heat. Although there was apparently some disagreement between Dr. Travell and the other White House physicians over methodology, JFK was put on a stretching and strengthening regimen for his back. In summary, Dr. Travell and her White House physicians left no therapeutic stone unturned.

Progressive Degeneration Of Tissues

Undoubtedly the most discouraging aspect of JFK's autoimmune disease to patient and physician was that he

was never able to really stabilize for any length of time. This is the nature of autoimmune disease. Unfortunately, autoimmune disease with its autoantibodies may continuously damage and destroy different tissue throughout a patient's life. Centralized pain is an inflammatory process in the brain that may progressively destroy tissue producing a variety of symptoms.[28,29] Today, we are much better able to control autoimmune disease mainly because we have laboratory tests that can monitor hormone levels, inflammation, and pain treatment effectiveness. Dr. Travell and JFK's other doctors simply had to "fly blind" in his medical management.

After Dr. Travell became JFK's primary physician in 1955, she and his other physicians had to regularly treat anemia, colitis, and infections. It is doubtful the doctors realized these various symptoms were connected, as the concept of autoimmunity had not yet materialized. He had to start daily thyroid hormone as his thyroid gland, like his adrenal glands, started to fail. In addition to bone, a most significant part of his progressive degeneration was his adrenal glands. At his autopsy, no adrenal gland tissue was grossly evident.[7] Microscopic sections from fatty tissue around his kidneys revealed only a few adrenal cells embedded in fat.[7] Obviously, his genetic autoimmune disease slowly and progressively over time ate away his adrenal glands just as Dr. Schmidt described in 1926.[17]

The Mystery Injections

A highly criticized activity within JFK's White House circle was that he would periodically see Dr. Max Jacobson, an émigré doctor from Germany. From his office in New York, Dr. Jacobson made a reputation for treating celebrities with "pep pills," which included amphetamine or a derivative. He reportedly prescribed some stimulants and injected JFK's back with a medication that he believed made him less dependent on crutches. Dr. Jacobson actually accompanied the Kennedy entourage to Paris to meet Charles De Gaulle in 1961, so he could continue giving the president injections. The nature of these injections is not recorded anywhere. When JFK was asked about them, he reportedly responded, "I don't care if it's horse piss. It works." This comment was probably literal. Assuming this to be true, the *Physician's Desk Reference* of 1955 lists injectable human chorionic gonadotropin, which, at that time, was extracted from the urine of pregnant mares.[34] This compound is now being used in patients with severe centralized pain, and many, like JFK, find it most useful. Its biologic effects are multiple and positive in a severe pain patient. It activates several hormones, dilates blood vessels, and produces soft tissue and nerve growth. The author knows of no other injectable drug that could have helped JFK as he was already receiving procaine, opioids, corticoids, and stimulants.

My Meeting With JFK

I met JFK when he and Hubert Humphrey came to Hutchinson, Kansas, to campaign in 1959. I was a student at the local junior college and these gentlemen spoke to us. JFK was a huge hit. Like most other persons who ever met him, he was warm, personable, and

Kennedy's Medical Material

John F. Kennedy's major medical facts are well catalogued and recorded, but they have been poorly understood from a pain management perspective. This article could only have been written due to some major medical reports written about JFK. In 2002, the trustees of the Kennedy Library opened up JFK's medical records for review to Robert Dallek and Jeffery Kelman, MD.[1,2] Their review and summary of his ills and sickness were expertly recorded in *The Atlantic* in 2002 in an article titled, "The Medical Ordeals of JFK." Dr. Kelman gave a most informative interview on PBS Newshour in 2002.[2] *The New York Times* published a most informative review of the records.[3] In 2009, Lee Mandell, MD, a Navy physician, published an article titled, "Endocrine and Autoimmune Aspects of the Health History of John F. Kennedy."[4] This article astutely describes the genetic disease that eventually led to JFK's development of centralized intractable pain.

Some Web sites have well chronicled the sequential health of JFK.[4,5] The physician who developed JFK's pain treatment from 1955 through his presidency until death was Janet Travell, MD. In 1968, she wrote a book on her White House experiences called, *Office Hours: Day and Night – The Autobiography of Janet Travell, MD*.[6] In it she describes her pain treatment for JFK. Lastly, George Lundberg, MD, and writer Dennis Breo of the *Journal of the American Medical Association* diligently pursued the facts about JFK's autopsy.[7,8] Known personally to this author, these were persistent ethical men who had no tolerance except for real facts. JFK's autopsy, particularly the finding that his adrenal glands had essentially disappeared, allowed an analysis and conclusion about JFK's pain history.

after shaking his hand you felt like he was a lifelong friend. Humphrey gave a rather dull 30-minute speech. JFK wowed us with a 5-minute talk. He was known for condensing political issues into short motivating speeches. At the time I made an observation, which I now recall. When he shook hands he stood very upright and when he sat at a table listening to Humphrey speak, he looked straight ahead and rarely turned or fidgeted like me. At the time I thought that he was simply a debonair disciplined man. Little did anyone suspect that he was a pain patient wearing a stiff back corset and taking multiple medications for intractable centralized pain.

Summary

Pain management practices are now seeing patients with genetic autoimmune diseases similar to that of JFK's. Unfortunately, autoimmunity may be a progressive lifelong disease that produces severe pain, which may become centralized in the CNS. Fortunately for JFK, he was referred to Dr. Travell for pain management in 1955. She was undoubtedly the best pain management physician at the time. Her treatment regimen was comprehensive and consisted of medication, exercises, and physical rehabilitation. It was the forerunner of contemporary treatment for severe centralized pain.

Writing in the *The Atlantic*, Dallek noted that Lee Harvey Oswald killed JFK before the president's medical ailments could.[1] In fact, Dallek surmises that "the evidence suggests Kennedy's physical condition contributed to his demise." On November 22, 1963, JFK was wearing a corset-like back brace as he rode in a caravan of official vehicles through Dallas. Oswald's first bullet struck JFK in the back of the neck. "Were it not for the back brace, which held the President erect [and not slumped over], the second, fatal shot to the head might not have found its mark," he concluded.

Despite this anecdote, it is clear that JFK would never have been in that convertible on that fateful day if it had not been for the skill of his pain physician. Practitioners of pain management as well as pain patients should study the case of JFK. There are many lessons to be learned. Above all, his pain story is one of great will, desire, and discipline on the part of both patient and physician.■

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Dr. Janet Travell, JFK's personal physician, in her White House office in 1961.

Pain Treatment—Then and Now

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I was lucky to get to know Janet Travell, MD, during the last 3 years of her life. We didn't communicate a lot, but I got the chance to see the incredible intelligence and commitment she had to patients. We mostly talked about the myofascial pain syndrome (MPS). She told me that it was her father who got her moving in that direction.

While I didn't know her very well, I was blessed to have a chance to talk with one of my medical heroes! People who have read my writings know I have done a lot of work with MPS, especially in association with various types of pain and acute and chronic tension-type headaches. I was very happy to have the chance to talk to her about my thoughts regarding the pathophysiology of some of these diatheses.

Dr. Travell's treatment of President John F. Kennedy was exceptional—treating him in an interdisciplinary way using the best medications available at the time. As noted in Dr. Forest Tennant's review, Dr. Travell's understanding of pain management was deep, and she used the available drugs both appropriately and for excellent reasons. For example, the treatment of JFK included hormones (testosterone and others). Knowledge of which hormones help to decrease pain, as discussed by Dr. Tennant, is not something that is widespread even today. Although the use of hormones did help with pain, it was also necessary to keep JFK alive and basically healthy (as well as could be expected with the autoimmune issues that were ongoing).

While it is certainly true that chronic peripheral pain can become centralized secondary to, among other issues, neuroplastic changes in the spinal cord (wide dynamic neurons) and in the brain, most of the medications used today to treat neuropathic or centralized pain did not exist when Dr. Travell was treating JFK—leaving her with only pain medications available. The drugs of choice today include anticonvulsant medications such as pregabalin (Lyrica), or even serotonin norepinephrine reuptake inhibitors like duloxetine (Cymbalta) and others, such as venlafaxine. These options were certainly not available 60+ years ago. Of the medications available to Dr. Travell, we know that meperidine and codeine (not used much at all today—if at all) were used for years for acute pain. We now understand (but probably not in the 1950s) that methadone has about a 10% N-methyl-d-aspartate receptor inhibition, which would have been helpful for analgesia of centralized pain.

Dr. Travell's use of sleeping aids (barbiturates) was both necessary, as well as a drug of the time. The same can be said for the meprobamate (another barbiturate)

and chlordiazepoxide (Librium) that Dr. Travell used for anxiety and as muscle relaxants. Her use of procaine injections was most likely into myofascial trigger points, a most helpful treatment that continues to be used today. The stimulant may have been used for both countering the sedative effect of the barbiturates and opioids, as well as to help decrease pain in JFK's central sensitization pain disorder. The use of gamma globulins in the president, who was dealing with significant hormonal deficiencies, was necessary. The use of vitamins B and C were also useful and certainly wouldn't harm the president.

'Bottom line—Dr. Travell treated President Kennedy in a highly appropriate fashion, using tools that most physicians today wouldn't know how to use, and even in ways they may not have been able to fathom.' *—Gary W. Jay, MD*

Finally, and most impressively, Dr. Travell treated more than the symptoms of pain and hormonal dysfunction. Her use of physical/physiatric measures (application of a heel lift, back brace, and corset) was very much needed. Even more importantly, Dr. Travell knew then what we know now—physical exercise is necessary to maintain a number of physiological functions as well as to help decrease pain.

If JFK was to be treated today, several changes would be made to the treatment plan. Regarding medication, the use of an extended-release opioid could be used. Methadone, of course, has an extended half-life, but many physicians don't know how to use it well. At issue is using extended release pain medications to make pain relief easier to obtain without "clock watching," which may include the use of a fentanyl patch or even oxycodone (Oxycontin).

Other medications for use as stimulants may not be needed with good pain management, but there continues to be methylphenidate for use, as well as amantadine, and others. There would be no issue with continuing to use procaine for injections into the myofascial trigger points. Lidocaine and benzocaine are also used.

Probably the biggest medication changes would deal with the hormones needed to address the autoimmune dysfunction JFK was dealing with. Transdermal testosterone by gel or patch is now common. Liothyronine (Synthroid) would be an appropriate treatment for his thyroid difficulties.

As Dr. Tennant noted, real cortisone for oral use was not developed until 1950. Today, hydrocortisone (Cortef) can be given orally for adrenal insufficiency. Also, today, of course, prednisone is readily available. The main issue here is that without cortisol and other adrenal hormones, the president wouldn't have been able to persevere either during the war, on a PT boat, or as president.

Muscle relaxants are different—meprobamate and chlordiazepoxide wouldn't be used today as true muscle relaxants. Probably the best drug for the long-term muscle spasm would be tizanidine (Zanaflex), an α-2 adrenergic agent. The use of the benzodiazepines as true striated muscle relaxants is not felt to be appropriate as the amount needed to actually induce striated muscle relaxation is far more than would be used for anxiolysis, and can induce significant sedation.

Sleeping aids, if needed, would today not consist of a barbiturate, but would be one of the newer drugs that interact with γ-aminobutyric acid–benzodiazepine receptor complexes, such as zolpidem (Ambien) or eszopiclone (Lunesta).

Bottom line—Dr. Travell treated President Kennedy in a highly appropriate fashion, using tools that most physicians today wouldn't know how to use, and even in ways they may not have been able to fathom. I do believe that Dr. Travell knew or intuited various things about drugs and hormones that we now understand better and more deeply. The fact that her treatment plan was so effective is a function of her exceptional skill as a physician at a time when physicians knew far less than we know now.

Dr. Travell was a very incredible physician as well as a person. I feel honored to have known her even for the little time I did.■