

A black and white photograph of Howard Hughes standing in front of a biplane. He is wearing a dark suit jacket, a white shirt, a tie, and light-colored trousers. The biplane is behind him, and the background shows a clear sky and a ground surface.

**Practical**

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# **PAIN MANAGEMENT**

*The journal with the practitioner in mind.*

**Diabetic Neuropathy  
Study**

**Occipital Nerve  
Stimulation for Migraine**

**Pregabalin for the  
Treatment of FMS**

**Use of TENS In  
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## **Howard Hughes and Pseudoaddiction**



# Howard

A retrospective case report of this remarkable individual's 30-year survival by self-medicating his intractable pain with codeine, anti-inflammatories, muscle relaxants, and stimulants—not as a drug-seeker, but as a “relief-seeker.”

With the emergence of opioid treatment of intractable pain (defined here as incurable, severe, and constant), there is great interest in the long-term survival of patients who require such treatment. At this time, there are no published reports of opioid-treated, intractable pain patients who have survived over a decade.

Because of a combination of fame and wealth, the revisiting of the Hughes case was made possible due to the volume of detailed public records available. Underneath the glamour, glitz, sex, money and politics that surround the saga of Howard Hughes, there is a serious and tutorial medical story from which all concerned parties can benefit. Hughes lived 30 years while taking high dosages of codeine in an average daily dosage between 20 and 45 grains a day. He survived a plane crash in 1946, developed intractable pain, and died 30 years later in 1976 due to specific anti-inflammatory agents that, over time, produced kidney failure.<sup>1-3</sup>

This author was contacted in 1978 by the U.S. Drug Enforcement Agency to be a consultant on Hughes. I was given copies of Hughes' autopsy report, post-mortem toxicology analysis, birth certificate, death certificate, a 1958 memo written by Hughes involving medication acquisition, and a daily log of medication administration kept by his aides and dated October 31, 1971 through July 1, 1973. These materials were presented in a public trial and are not confidential documents.<sup>3</sup> This log, covering his habits and behavior in detail, was in the 25th and 26th year after his plane crash and continuous consumption of opioids. It is very revealing as to how he treated his pain and continued to function.

In September 1978, this author compiled a written report for the U.S. Government based on the aforementioned documents. In addition, this author appeared as an expert witness in the Ogden, Utah Federal trial, U.S. versus Thain (Hughes' physician in the last years of his life)<sup>3</sup> and was able to interview two of Hughes' now-deceased, personal physicians about Hughes' medical history and treatment.

It is cogent to point out that in 1978, this author was fully vest-



# Hughes

# PSEUDOADDICTION

by Forest Tennant, MD, DrPH

ed in addiction research and treatment and had only begun to research and treat intractable pain patients with opioids. Consequently, the resulting 1978 analysis of this matter, including terminology and biologic concepts, were archaic given the monumental, historic, and scientific breakthroughs in the understanding of addiction and pain that have occurred since 1977.

Due to the great interest in the long-term survival of pain patients treated with opioids, a re-analysis and report of Hughes at this time is most informative and instructive for physicians and patients. This re-analysis incorporates many of the current terms, concepts, and scientific advances that have emerged in the past 30 years. To provide perspective on how pain management has matured since that time, some relevant terms are shown in Table 1.

### Precipitating Cause of Pain and Initiation of Opioid Treatment

Born in 1905, Hughes was a world-recognized, pioneering entrepreneur engaged in diverse businesses that included chemicals, plastics, moving pictures, entertainment, and aircraft design and development. In 1946, at the age of 41, Hughes solo-tested an experimental reconnaissance plane known as the XF-11. Shortly after take-off from the Santa Monica, California airport he crashed. He miraculously survived the crash and was immediately hospitalized at Good Samaritan

TABLE 1. SOME PAIN TREATMENT CHANGES IN TERMINOLOGY AND CONCEPTS DURING THE PAST 30 YEARS		
	1977	2007
<b>Addict</b>	An addict was anyone who took a prescription drug in dosage above the usual frequency or for an extended duration	An individual who compulsively uses a substance for non-pain purposes
<b>Pseudoaddiction</b>	Term not used	Syndrome in which an individual who seeks drugs for pain relief since their pain is out of control
<b>Intractable</b>	Term not used	Incurable, severe, constant pain
<b>Breakthrough Pain</b>	Term not used	A flare of pain above the usual baseline pain level
<b>Short &amp; Long-acting Opioids</b>	Terms not used	Usual treatment for severe intractable or persistent pain is a long-acting opioid plus a short-acting one for breakthrough pain
<b>Pain Characterization</b>	Essentially none	Common classes include neuropathic, myofacial, and reflex sympathetic dystrophy
<b>Effect of Renal Failure on Drug Serum Levels</b>	Little understanding	Poor renal clearance may greatly raise serum levels of therapeutic drugs
<b>Morphine Equivalency</b>	Unheard of	Pain potency of all opioids are equated to the effect of 1mg of morphine

**TABLE 2 . INJURIES SUSTAINED BY HUGHES IN 1946 PLANE CRASH THAT LIKELY PRODUCED INTRACTABLE PAIN**

- Third degree burn of abdomen and chest wall
- Fractures of chin, jaw, left knee, and left elbow
- Multiple burns of left ear, left chest, left abdominal wall, little finger left hand, left buttocks
- Third degree burns in some areas. One large burn extended from his left shoulder to left hip
- Displacement of 6th cervical vertebrae onto the body of the 7th
- Fracture through lateral articular facets of 5, 6, 7th cervical vertebrae
- Fractures of ribs 1, 2, 3, and 4 on right. Fractures of 1, 2, 3, 4, 5, 6, 7, 8, and 9 on left
- Fracture of left clavicle
- Hemorrhage into left chest cavity with displacement of heart into right chest
- Hemorrhage into mediastinum
- Blood loss requiring transfusions

Hospital in downtown Los Angeles. His injuries were numerous and included multiple fractures and third degree burns (see Table 2). He required three chest drainings, since he recurrently bled into his left chest cavity. Four skin grafts were required to close a large third degree burn extending from his shoulder to hip. He remained at Good Samaritan Hospital for about 5 weeks between July 7 and August 11, 1946. Hughes was given morphine while hospitalized and was discharged on codeine. A detailed list of Hughes' injuries are listed in Table 2 to emphasize that essentially no one can survive these injuries without developing intractable pain.

Modern day pain treatment specifically and clearly recognizes that neck and facial fractures are associated with intractable pain. Third degree burn scars are known to cause pain in peripheral nerves. Pain that radiates from a central nerve injury into the face, arms, legs, or chest wall is now referred to as neuropathic pain. This term was not used during the life of Hughes. Details of his injuries are given here to eliminate any misconceptions and refute some public reports that he didn't have pain that required ongoing medication.

### Characterization of Hughes' Pain

Today's pain terminology, as confusing and deficient as it may be, helps provide a framework to understand Hughes and all other pain patients. Acute pain is one of sudden onset and that resolves within

days or weeks. A headache is a good example. Chronic pain is an intermittent or constant pain that persists beyond about 90 days. Millions of people suffer from mild or moderate chronic pain due to such causes as arthritis, lumbar sprain, bunions, or carpal tunnel.

The severe form of chronic pain is more and more being referred to as "intractable pain." This form of chronic pain is reserved for those severe chronic pain patients whose pain is severe, incapacitating, constant, incurable, and interferes with biologic functions including sleep, eating, ambulation, and social interaction. Undertreatment results in reclusivity and a home or bed-bound state. Intractable pain patients have a persistent or baseline pain with flares or breakthrough episodes above their baseline pain. Injuries such as those sustained by Hughes in his 1946 plane crash inevitably produce chronic pain and likely cause intractable pain. Scientific studies now show it is usually possible to separate intractable pain from ordinary chronic pain in that intractable cases present demonstrable biologic changes in heart rate, blood pressure, and adrenal hormone production. Analysis of Hughes' medical and pain history clearly shows that today he would be characterized as an IP patient.

Hughes' pain, according to his physicians, was constant and centered around his neck, shoulders, back, and into his arms. In the 1946 plane crash, he suffered fractures of some cervical neck facets. Collapsed vertebrae were noted on x-rays

taken at autopsy. His physician in the last years of his life, Dr. Wilbur Thain, described his skin as "extremely sensitive to touch" and any cutting of his finger or toe nails "hurt like hell."

As Hughes aged, he developed degenerative arthritis in several joints that aggravated his pain. After his fractured left hip was pinned in 1973, he did not walk again and developed a contracture of the left leg. His hip fracture and contracted leg may also have contributed to his pain. Dr. Thain offered Hughes a walker, wheelchair, and even a cute physical therapist to help him walk again. Hughes replied humorously to the latter, "No Wilbur, I'm too old for that." Thain considered, and rightly so, that Hughes' resistance to walking after his hip fracture was "the beginning of the end." Modern day pain specialists ask and demand physical activity and movement from intractable pain patients if they are to escape a bed or couch-bound state. In this regard, Dr. Thain appeared to be a physician well ahead of his time.

Hughes suffered several neuropathies and had allodynia which presents as severe pain to the touch. He would possibly today be given the diagnosis of Reflex Sympathetic Dystrophy or Chronic Regional Pain Syndrome. At times, his pain was reported to be so severe that a simple touch or the touching of bedclothes produced pain. His renowned refusal to brush his teeth, cut his toe and finger nails, or wear shoes may have been related to the fact that these actions may have caused increased pain.<sup>5,6</sup> His multiple facial fractures probably produced a neuropathy of his jaws and face. At this time, it is not possible to correlate his pain and its treatment to any impact on his renowned, lifelong eccentricity and obsessive-compulsive traits or to his failure to brush teeth, cut nails, or exercise.<sup>5,6</sup>

### Pseudoaddiction or Addiction?

After Hughes' death and the revelation that he had taken high dosages of codeine and diazepam (Valium®) for many years, he was mistakenly labeled an addict by all concerned parties—including this author. In addition, he was assumed to abuse his medications since reports indicated he became over-sedated with resulting pressure (bed) sores, falls, reclusivity, and obsessive-compulsive traits such as over-washing. To compound this belief, a memo was written by Hughes in 1958

which gave detailed instructions to his aides on how to obtain controlled drugs. This memo was initially believed to be a surreptitious attempt to obtain drugs for purposes of abuse, but later information revealed that it was simply to obtain medications legitimately prescribed by his physicians. His major physician at this time was Dr. Vern Mason, an accomplished internist who cared for Hughes' pain in the early years after the plane crash, and prescribed codeine. His physicians instructed him on how to inject codeine.

Today, Hughes' drug seeking would be termed pseudoaddiction, not addiction. There is now a standard set of terms adopted by all major professional pain treatment organizations and the American Society of Addiction Medicine. New terms and definitions propagated by the National Federation of Medical Boards are critical to the understanding of Hughes' pain and medical catastrophe, and so they are given here:

**Addiction.** Addiction is a primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include the following: impaired control over drug use, craving, compulsive use, and continued use despite harm.

**Pseudoaddiction.** The syndrome results from the misinterpretation of relief seeking behaviors as though they are drug-seeking behaviors commonly seen with addiction. The relief seeking behaviors resolve upon institution of effective analgesic therapy.

**Tolerance.** Tolerance is a physiologic state resulting from regular use of a drug in which an increased dosage is needed to produce a specific effect, or a reduced effect is observed with a constant dose over time. Tolerance may or may not be evident during opioid treatment. Physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and are not the same as addiction.

**Chronic Pain.** Chronic pain is a state in which pain persists beyond the usual course of an acute disease or healing of an injury, or that may or may not be associated with an acute or chronic pathological process that causes continuous or intermittent pain over months or years.

**Physical Dependence.** Physical de-



**FIGURE 1.** This x-ray taken at autopsy shows 5 needles imbedded in Hughes' arms. Just as diabetics did in those days, Hughes had to self-inject codeine intramuscularly with outmoded glass syringes that had detachable needles which frequently came loose under the skin. When this x-ray was first observed, an erroneous conclusion was made that it indicated addiction and abuse of codeine rather than pseudoaddiction. Hughes' best pain relief was by injecting codeine, but codeine was probably not nearly potent enough to fully relieve Hughes' pain.

pendence is a state of adaptation that is manifested by drug class-specific signs and symptoms that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. Physical dependence, by itself, does not equate with addiction.

There is no more profound example of misinterpretation relative to addiction versus pseudoaddiction than the finding of 5 imbedded needles seen on Hughes' arm x-rays taken at autopsy (see Figure 1). After seeing these x-rays, the immediate—and mistaken—conclusion by this au-

thor and others was that the embedded needles must represent addiction and abuse of drugs. Later understanding of the effectiveness of oral versus injectable opioid compounds reveals the true picture. Hughes self-injected pure codeine phosphate and also took oral compounded codeine (i.e. codeine with phenacetin, aspirin, etc.). In later years Hughes' physicians confirmed that his major pain relief was by injectable codeine. It is now clear that codeine would not be potent enough or last long enough in the body to provide much pain relief for Hughes. For example, codeine's effective pain re-

**TABLE 3. LIKELY COMPLICATIONS OF HUGHES' INTRACTABLE PAIN**

- Osteoporosis, scoliosis, and vertebrae collapse
- Tooth erosion
- Hormone alterations

\* *The above may have been partially caused by other factors such as being non-ambulatory and uremic in his last four years of life.*

lief activity is seldom over about 3 hours, and Hughes obviously required pain relief 24 hours each day. These simple facts give ample reason for a high daily dosage of codeine. Imbedded needles are easy to understand when one realizes that there were no disposable syringes with attached needles in Hughes' day. Syringes used today by pain patients are disposable after one use, sanitary, plastic, and have sharp small attached needles to prevent imbedding. Hughes had to use a glass syringe with non-attached needles that easily came loose when injected. The same also applied to diabetics in those years who also commonly left needles under the skin.

It is worth noting that Hughes did not have the usual addictive personality witnessed in America. He did not smoke cigarettes and seldom drank alcohol. He did not routinely inject codeine by the intravenous route as would an addict but, instead, he injected it into the subcutaneous and muscular tissues.

### Complications of Intractable Pain

It is now known that intractable pain, per se, will produce complications, and Hughes appeared to suffer some (see Table 3). The most physical demonstration was osteoporosis and teeth erosion. Intractable pain, when uncontrolled, produces hypercortisolemia and loss of bone and teeth composition. Osteoporosis combined with the sedation of diazepam appeared to contribute to his 1973 fall and hip fracture. Further, collapsed vertebrae of the neck were seen on x-ray at autopsy. His pain also likely contributed to his tendency to reclusivity. Today we inquire of intractable pain patients as to whether their baseline pain and flares are causing them to be bed or house-bound. His out-of-control pain likely also caused him to refrain from some types of physical activities or exercise.

Intractable pain is now known to cause

profound alterations in hormone production. In addition, opioid drugs will decrease testosterone production. Uncontrolled pain seems to decrease the ability of nerves to function. Hughes had difficulty urinating which is typical of intractable pain patients both due to spinal nerve injury and opioid drugs. According to Michael Drosnin in his excellent book, *Citizen Hughes*, Hughes quit womanizing about 15 years before his death.<sup>5</sup> He also divorced about this time. Considering the severity of Hughes' pain and his necessity for potent medication, this time-point in his 30-year survival appears valid. Today, intractable pain patients are given hormone replacement to help carry on marital life.

The daily log kept by Hughes' aides between 1971 and 1973 provide evidence that he was tolerant to codeine and was functioning quite well but that he also suffered from complications of intractable pain as well as his medications. There is no mention of any female visitors or of him leaving his quarters to see a female. Evidence for osteoporosis, scoliosis, and collapsed vertebrae is found. Hughes had to sleep in a partial sitting position. He required a "two pillow-pillow." A very hard pillow was in the pillow case to be next to his back and a regular pillow was on top to be placed against neck and head. The log ends at the time he fell, fractured his hip, and entered a London hospital.

### Codeine Treatment and Complications

Following his 1946 plane crash and hospitalization, Hughes apparently self-administered codeine almost daily after leaving the hospital up until his death 30 years later. Except for a few days just prior to death when Hughes was unable, he self-administered all his medication and was alert enough to do so. His medication supplies were in his room. The daily log between 1971 and 1973 indicated that aides were often aware of how much and

when medication was self-administered, but there is no record that aides themselves routinely administered medication. In the few days prior to death Hughes', when Hughes was incapacitated, his aides apparently administered some codeine, because codeine was in Hughes' body at autopsy. No other drugs were present. There is no medical evidence that Hughes' aides or doctors intentionally attempted to over-or under-medicate Hughes. He self-administered two forms of codeine. One was codeine phosphate which could be dissolved and injected, and the other was various oral formulations of codeine compound which consisted of phenacetin, salicylamide, acetaminophen, aspirin, and caffeine. His initial starting dosages of codeine and his split between oral and injectable codeine are uncertain but varied over time. Hughes and his physicians confirmed, however, that he usually consumed an average of between 20 to 45 grains (1200 and 2700mg) a day during most of the 30 years. Some daily dosages may have reached 60 grains (3600mg) a day. The activity log kept between 1971 and 1973 reveals that he could take 8-10 codeine (480 to 600mg) at one time indicating considerable tolerance and longtime use of codeine.

As mentioned previously, codeine's pain relief duration is seldom over 3 hours and so gives ample reason for Hughes' high daily dosage of codeine. While the number of grains (20 to 45gr) or equivalent milligrams (1200 to 2700mg) sound high, codeine is such a weak opioid that Hughes could not possibly have been able to always control the severe, intractable pain that likely resulted from his plane crash. About 10mg of codeine are equivalent to 1mg of morphine, so Hughes was taking the potency of about 120 to 270mg of morphine a day. This is a low to moderate dose for many of today's intractable pain patients. Today it is not uncommon for the daily morphine dosage to exceed 1000mg a day or a daily dosage 4 to 5 times more potent than the opioid dosage taken by Hughes.

In an effort to achieve some modicum of pain control, Hughes suffered considerable complications from the use of codeine. The phenacetin in the codeine compound produced, over time, kidney failure and death. He endured severe constipation and hemorrhoids which are well-known complications of codeine. He



frequently had to resort to enemas for relief of constipation and he suffered intermittent rectal prolapse. His physicians had to periodically reinsert his rectum.

In summary, Hughes probably received inadequate pain relief from codeine, and he suffered severe complications from it (see Table 4). In addition, his poorly controlled pain likely interfered with his business and social life. Due to codeine's weak pain relief and numerous complications, it is essentially not used today for intractable pain treatment. Several other opioids are now available which give superior pain relief with fewer complications.

### Anti-Inflammatory Treatment

Hughes also constantly self-administered anti-inflammatory agents following his plane crash. These agents were in the codeine compounds that he took orally and contained various quantities of phenacetin, aspirin, salicylamide, acetaminophen, and caffeine. However, in the months just prior to his death, he used a simple aspirin and codeine combination.

This author believes that the anti-inflammatory agents used by Hughes helped enhance his pain relief and promote his longevity. Despite the likely benefits, Hughes suffered typical complications of excess anti-inflammatory agents. He had multiple bouts of gastrointestinal bleeding and anemia to the point he required blood transfusions. In the weeks just prior to his death, his physicians attempted to increase his aspirin dosage and reduce his codeine dosage. This problem accelerated his chronic renal disease caused by phenacetin. At autopsy, there was papillary necrosis of the kidneys which is commonly caused by excess aspirin. A gastric ulcer was present at autopsy which was also likely caused by excess anti-inflammatory agents.

The renal deterioration produced by Hughes' anti-inflammatory drugs, principally phenacetin, began several years before his death. Just how long he was uremic is unknown. It is very likely that much of his inactivity, irascible behavior, and sedation in the decade prior to death was caused by uremic poisoning. Hughes kidneys weighed only about 100 grams each at autopsy, compared to a normal weight of 450 to 600 grams each.<sup>7</sup> Also, Hughes apparently didn't need to use codeine on a regular basis in his terminal months as his kidneys progressively failed and couldn't rapidly eliminate codeine from the body. Just two days prior to death, and at autopsy, he had blood urine nitrogen levels of 47 and 60mg/dl while the normal range is 8-24mg/dl. These laboratory findings confirm long-time, progressive, renal failure.

### Benzodiazepine (Valium®) Treatment

In the 1960's, after diazepam came on the commercial market, Hughes began using it. It is unknown as to the precise reasons he began this agent, but he continued it until he fractured his hip after a fall in July, 1973. The daily activity log kept by aides between 1971 and 1973 revealed that Hughes took between 7-15, 10mg diazepam per day. His aides referred to the blue 10mg Valium® tablets as "blue bombers" apparently due to their potent sedative effects.

Hughes was admitted to a London hospital for hip pinning in 1973. Undoubtedly his fall and hip fracture were related to his excessive diazepam use since this occurrence is well known to happen in elderly persons who use benzodiazepines to excess.

**TABLE 4. DRUG-RELATED COMPLICATIONS EXPERIENCED BY HUGHES OVER 30 YEARS**

#### Opioid — Codeine

- Constipation
- Hemorrhoids
- Rectal prolapse
- Imbedded needles
- Difficult urination

#### Benzodiazepine — Diazepam

- Over-sedation
- Falls
- Fractured hip
- Pressure sores

#### Anti-inflammatory Agents — Phenacetin, Aspirin, Acetaminophen, Salicylamide

- Gastrointestinal bleeding
- Peptic ulcer
- Renal atrophy/failure

*Hughes suffered and endured tremendous complications of the drugs he had to use to control pain and allow physical and social functions during his 30-year survival.*

In addition to his tragic fall and fractured hip in 1973, Hughes appeared to suffer from bouts of over-sedation due to his benzodiazepine use. On several occasions Hughes developed pressure sores on his buttocks and shoulders. He would reportedly sleep for 24 to 48 hours on some occasions.<sup>6</sup>

Although Hughes' hip was apparently successfully pinned, Hughes refused physical therapy and declined to walk or leave his bed the last four years of his life. This information comes from his doctor's declaration, since there are no log or medical records about Hughes after 1973. In this author's clinical experience, intractable pain patients will refuse to walk, exercise, or leave bed until, and unless, their pain is well-controlled. Hughes had scars due to his 3rd degree burns as well as many damaged nerves throughout his body. One cannot simply tell patients to exercise or send them for physical therapy since, depending on their individual circumstances, exercise or stretching may increase pain. This author, in his intractable pain practice, has had to tailor a stretching and exercise program for each patient—often after reviewing magnetic resonance imaging (MRI's) x-rays to know what is safe and won't cause more damage. It is suspected that Hughes did not exercise or leave his bed because it caused him additional pain, and his doctors would not have known how to create a special exercise program in those days. After Hughes had his hip pinned in 1973, no evidence can be found that his physicians continued diazepam. If this were the case, his pain would undoubtedly accelerate, since codeine and anti-inflammatory agents wouldn't suffice for very good pain control.

Hughes claimed that diazepam helped him sleep. Diazepam will also suppress opioid withdrawal symptoms which may occur

**TABLE 5. VERBATIM WORDING FROM HUGHES' AUTOPSY DONE AT METHODIST HOSPITAL IN HOUSTON, TEXAS IN APRIL 1976, REGARDING HIS BRAIN**

**BRAIN AND SPINAL CORD**

The dura is intact and no evidence of epidural or subdural hematomas, recent or remote, are found. The brain weighs 1540 grams (Normal range is 1380 to 1590 grams<sup>7</sup>). The cortical surfaces show no lesions. The basilar cerebral vessels are with usual anatomic distributions with the exception that only one vertebral artery is present, situated on the left. No aneurysms are noted at any of the bifurcations. Athromatous involvement is minimal. No evidences of cingulate, uncus or cerebellar tonsillar herniation is present.

Multiple 0.5+ 1.5 cm thick transections of the cerebrum, cerebellum and brain stem show no abnormalities of the cortex, white matter, thalamus, cerebellum, pons or medulla. Modest dilation of the occipital poles of the lateral ventricles is present. The foramina of Monroe are patent. The third ventricle, aqueduct of Sylvius and 4th ventricle are not dilated. The spinal cord shows no gross abnormalities.

**CEREBRUM**

Slight fibrosis of leptomeninges. Precentral cortical grey matter reveals well preserved motor neurons. There is no evidence of accelerated involutinal changes of the cerebral cortex.

**DIENCEPHALON AND BRAIN STEM**

Thalamus and inferior olivary nucleus show hypertrophic astrocytes (Alzheimer type II), consistent with metabolic changes.

**SPINAL CORD**

Not remarkable.

**DIAGNOSIS**

No diagnosis.

*Hughes' brain at autopsy was normal and showed no atrophy or changes due to his pain or medications. These findings support his long-term treatment approach.*

**TABLE 6. KEY AUTOPSY FINDINGS**

- Normal Brain, Adrenal, Testicle, Liver, Spinal Cord
- Coronary Heart Disease
- Generalized Osteoporosis
- Renal Atrophy/Papillary Necrosis
- Gastric Ulcer
- Fracture of Left Old Hip with Metallic Pin
- Collapsed Vertebrae and Scoliosis

*The autopsy, x-rays, and toxicologic analysis taken after death confirms the various physician reports about his complications of intractable pain and the drugs he took.*

between codeine dosages. Diazepam and other benzodiazepines produce muscle relaxation and some relief for the neuropathic pain that Hughes had. Diazepam is known to enhance opioids' pain relieving capability. Hughes undoubtedly took excess diazepam from time-to-time since codeine was not adequately relieving his pain.

**Autopsy Findings**

The autopsy of Hughes is especially of great interest to pain practitioners since none other is available for a 30 year intractable pain patient treated with opioids. Of special note is that the gross and microscopic analysis of his brain, adrenals, testicles, and liver, were reported as normal. Some early studies of uncontrolled pain had suggested that brain atrophy may occur. There is also the misconception that opioids and other pain control medications may cause brain damage. Consequently, a detailed description of brain findings from his autopsy, done at "The Methodist Hospital" in Houston, Texas, is given here for the sake of current and future investigations by researchers. Table 5 provides precise quotes from his autopsy report. To verify the authenticity of the autopsy report given to this author by the Federal Government, it is on Methodist Hospital stationery and signed by two physician pathologists. The report additionally contains notes from a 3rd pathologist and a dentist.

The nervous system findings in Hughes show remarkable normalcy for his 70-year age and indicates that many things went "right" over the 30-year pain period. Certainly his medications did not distort brain anatomy. There was no reported evidence of tertiary syphilis that was widely reported in the press. Late stage syphilis would have appeared in liver and brain, but there was no such evidence found. Late stage syphilis produces a very distinctive, obvious lesion in brain, liver, and spleen known as "gummas," because they look like wads of gum. None were present in Hughes. Even if Hughes had contracted syphilis in his early life, penicillin became available in the early 1940's, and only a few dosages would kill syphilis. Hughes had received antibiotics several times over the years, so any syphilis would have been eradicated.

His autopsy clearly showed end-stage renal disease. There were two types of



damage. One was generalized atrophy of the type caused by chronic phenacetin use. The other was acute papillary necrosis caused by anti-inflammatory agents and likely related to his physician's attempt to decrease his codeine use and substitute aspirin in the few months just prior to his death. A gastric ulcer was present which was also likely caused by an excess of anti-inflammatory agents.

Other cogent findings at autopsy (see Table 6) included numerous old scars and fractures related to his plane crash. Severe teeth erosion was present. Roentgenograms showed osteoporosis, collapsed cervical vertebrae, scoliosis, and five imbedded needles in his arms (see Figure 1). One coronary artery had 60% occlusion. This finding is typical of a 70-year old person, so it is difficult to relate this finding to either his pain, diet, or drug intake.

A curious finding was the presence of only one vertebral artery rather than two. This intriguing and unusual finding may be a tracer or indicator of unusual brainpower, and Hughes certainly demonstrated a most amazing intellect, including his ability to survive 30 years with intractable pain.

Toxicologic analysis at autopsy showed only codeine with no benzodiazepines, phenacetin, salicylates, or alcohol. The codeine concentration in the blood was 1.96mg/liter. Much debate as to the meaning of this concentration ensued immediately after his death. There was the belief, as published in some national newspapers, that this level meant that Hughes was given a lethal injection just prior to his death for surreptitious purposes. This reaction is understandable, since there were no studies of opioid blood levels in intractable pain patients in 1976. There was limited data on overdose deaths due to codeine in 1976 and what little was available revealed that Hughes' codeine blood level was within ranges observed in codeine overdose deaths. What was not appreciated was that pain patients who chronically consume opioids develop tolerance and can maintain very high blood levels and yet function very well.<sup>4</sup> Recent opioid blood studies show that Hughes' codeine blood level of 1.96mg per liter to be quite compatible with his usual intake of codeine. In addition, his kidneys were failing and, therefore, blood levels would be artificially high since his kidneys had impaired

**TABLE 7. POSITIVE LONGEVITY FACTORS IN HUGHES  
30 YEAR SURVIVAL**

1. Immediate initiation and continuation of opioids after plane crash
2. Opioid - High Dose Codeine
3. Benzodiazepine - Diazepam
4. Anti-inflammatory Agents - Phenacetin, Aspirin, Salicylamide,
5. Stimulant - Caffeine
6. High Protein Diet - Chicken, Milk
7. Non-smoker, little alcohol
8. Mind Occupied with Business, Movies
9. Will-to-Live
10. Sense of Humor
11. Excellent physicians
12. Vitamins and minerals

*Above are the author's personal opinions as to some of the factors that helped Hughes survive 30 years against incredible odds.*

excretion. Hughes' codeine blood level at autopsy does, however, help validate the reports by his physicians relative to Hughes' usual codeine intake.

### **Functionality And Social Contributions While In Pain**

Even though Hughes began regular high dose opioid use in 1946 after his plane crash, many of his legendary accomplishments occurred after this time. A partial list includes the development or production of the Spruce Goose, Glomar Explorer, RKO Studios, Hughes Aircraft, Howard Hughes Medical Institute, and Las Vegas Casinos. He eloquently spoke at Senate hearings in 1948. He married Jean Peters in 1958.<sup>1,2,5,6</sup> These accomplishments are compatible with numerous reports in recent years showing that many persons who are tolerant to daily, high dose opioids and who demonstrate high opioid blood levels function quite well physically, mentally, and socially.<sup>4</sup> The author does not claim to be an authority on the social and business life of Hughes except to clearly emphasize that severe intractable pain and treatment with high opioid drugs is compatible with a productive, happy life. Once opioid tolerance is achieved, pain relief and essentially normal mental and social function is present. The stereotype of Hughes as an over-sated, bumbling, unproductive, germ-chasing drug addict is simply false. The logs kept between 1971 and 1973 clearly

reveal that Hughes could function quite well with his high dosages of codeine, anti-inflammatory agents, and diazepam (Valium®). In this two year period, log entries show that he regularly transacted business including stock sales, leases, and tax decisions. On one occasion, he left his hotel to fly an airplane. On March 13, 1972 he met with President Somoza of Nicaragua. The log also recounts the famous telephone interview on January 7, 1972 regarding the fraudulent Clifford Irving biography and later signing affidavits for the New York Supreme Court. He regularly read newspapers in addition to movie screenings. He made several trips and stayed in numerous locations including Managua, Miami, Vancouver, and London.

This report is not able to precisely correlate Hughes' renowned reclusivity with his pain, opioid use, or treatment complications. Uncontrolled or poorly controlled intractable pain, however, is well-known to result in a bed or house-bound state. This report is also unable to correlate any positive or negative affects of his pain or treatment drugs on Hughes' well-known lifetime obsessive, compulsive, and eccentric traits.<sup>5,6</sup> The two year daily log indicates that his only obsession was to have lots of kleenex by his bed. There is no mention of hallucinations or delusions. Indeed, Hughes' traits may have been overblown in the press, since his physicians all agreed that he was eccen-

tric and sometimes irascible, but never hallucinated or exhibited psychotic behavior.<sup>2</sup>

### Positive Longevity Factors In Hughes' 30-Year Survival

Several factors likely helped Hughes survive 30 years (see Table 7). First, he hired and retained excellent personal physicians who provided regular medical attendance and consultation over his 30-year survival period. Despite Hughes' reclusivity, geographic mobility, and hotel accommodation, his personal physicians had access to him. The connotation in some of the lay literature about Hughes' physicians and the criminal charges brought against some of them give the erroneous impression that his MDs were second rate. Not so. They had outstanding pedigrees and long-time clinical experience. Additionally, most were older than Hughes. Dr. Thain was totally exonerated at his trial and he gave, before a jury, a detailed and complete story of Hughes' medical condition and treatment based on the latest medical information available at the time. My review of Hughes indicates that his MDs were about the only persons he confided in about his true feelings and personal matters. In contrast to the uncaring, ruthless, and purely business persona perceived by the public, Hughes often discussed his life, pain, and fears with his doctors. Dr. Thain related that Hughes often expressed how he loved his mother and father, as well as Jean Peters, his last wife. Despite their divorce, this love must have been reciprocal, because Ms. Peters was essentially the only person to send flowers for Hughes' grave after he died. Although, more often than not, Hughes rejected his physicians' advice, all accounts that the author can find indicate a close personal, physician-patient relationship between Hughes and his doctors. His doctors encouraged him to endure and this probably contributed to his 30-year longevity. When asked if Dr. Thain regretted caring for Hughes he replied, "He had no one else, and I could not have walked away from him." Indeed, when Hughes lay in the funeral home waiting to be buried, not a single person came to visit and only a handful of family members were at the gravesite.

Hughes had an incredible lust for life and will to live. Within about two hours after Hughes' plane crash he was receiving blood transfusions and his long-time

physicians, Dr. Verne Mason (internist) and Dr. Lawrence Chaffin (surgeon), started draining his chest cavity. Hughes asked Dr. Mason, "How am I doing?" Mason replied, "I'm not going to lie to you, Howard, you might not live." In response Hughes reportedly stated, "Do what you can, I'm prepared."<sup>1</sup>

Dr. Mason later gave a press statement exclaiming, "My patient is truly 'The Man of Steel,' and he is crawling back to health from injuries that would have killed most men. He's not out of danger yet, but he has a terrific will to live. That alone might save him."

While it is scientifically impossible to precisely correlate will-to-live and lust-for-life attitudes with intractable pain and longevity, these attitudes must have been enduring and surely have been a foundation for Hughes' 30-year survival. Hugh-

usually has a genetic basis. The only recorded blood pressure known to the author was in 1973 at the time he had his hip pinned. It was 124/72mmHg.

Major factors in his survival undoubtedly were that he did not smoke and seldom drank alcohol. On the negative side, there is no record of any physical therapy or desire to participate in much physical activity or exercise. He voluntarily chose to remain bed-bound for four years after his hip was pinned in 1973, and he apparently refused his physicians' advice to exercise or stretch his left leg. Hence he developed contractures and likely increased knee pain. I am unable to explain Hughes' apparent aversion to exercise and physical therapy, unless it is related to poor pain control.

Hughes' medical regimen was elementary and hazardous, although it contained

*"Hughes' medical regimen was elementary and hazardous, although it contained the major medical components of modern day chronic pain treatment. It consisted of an opioid, anti-inflammatory agents, stimulant, and a benzodiazepine."*

es apparently was ready for death but vigorously sought to postpone it. This attitude is a good one for IP patients.

Dr. Mason was the internist who prescribed codeine after his plane crash. In those years (40's, 50's, and 60's) there was no social stigma, "big deal," or controversy about opioids for pain relief as there is today. At one interview, Dr. Mason simply said, "I continued prescribing codeine because Mr. Hughes needed it." The immediate implementation of continuous opioid therapy following the plane crash was probably paramount to Hughes' survival. There is an emerging body of scientific evidence that says acute pain from injury or surgery should be aggressively treated early and continuously until the pain is gone, lest the injury and pain progressively worsen.

Hughes remained lean and apparently maintained a normal blood pressure. Hughes did suffer from attacks of high pulse rate as high as 200 to 240 beats per minute. This condition, known as recurrent paroxysmal tachycardia, would respond to carotid pressure. Pain flares are known to precipitate this condition and

the major medical components of modern day chronic pain treatment. It consisted of an opioid, anti-inflammatory agents, stimulant, and a benzodiazepine. Codeine, although a weak opioid, was taken in high enough dosages to likely maintain a reasonable serum concentration for pain relief, particularly when taken by injection. The high dosages of the anti-inflammatory agents phenacetin, salicylamide, aspirin, and acetaminophen undoubtedly had some therapeutic, longevity, and pain-relieving effects—despite their significant complications, including renal failure, that was Hughes' ultimate cause of death.

The role of caffeine is unclear. Although he apparently drank few, if any, caffeinated beverages, he consumed considerable caffeine in his codeine compounds. Caffeine is known to potentiate or enhance codeine's pain-relieving ability. Caffeine is also a good antidepressant, energizer, and motivator. Today's modern pain treatment is starting to use a number of stimulant compounds to enhance treatment.

Of great interest is Hughes' diet. He

liked protein and constantly consumed chicken including chicken soup. He drank considerable milk. The daily activity log kept by his aides between October 31, 1971 and July 1, 1973 indicates he ate protein in the form of chicken essentially every day. Some notes indicate turkey sandwiches were eaten and he ate steak at times.<sup>5</sup> Protein contains amino acids which are the body's natural building blocks for tissue, nerves, and various neurotransmitters. This author has observed that intractable pain patients who eat considerable protein and take multiple dietary supplements have far better pain control and function better than patients who do not practice these measures. Although little scientific study can yet back

### What We Would Do Medically Differently Today?

There are many therapeutic things we would do differently now—thanks to scientific advances—but Hughes' fundamental pain treatment program, however, was basically sound: opioid (codeine), anti-inflammatory agents (aspirin, etc.), muscle relaxants and sleep medication (diazepam), and stimulant (caffeine). No wonder he made it 30 years with intractable pain, despite a weak opioid as his major pain reliever. Rather than weak, short-acting codeine, we would today prescribe a long-acting opioid with fewer side-effects for his baseline, persistent pain and a short-acting, opioid for breakthrough pain or pain flares. There are

*“The big lesson is that if Hughes could live 30 years with the poor pain treatment available to him, current IP patients—given modern intractable pain treatment and testing—should easily equal and likely exceed that while maintaining a reasonable quality of life.”*

up this statement, it is appropriate to point out that the body's natural endorphins and opioid receptors are composed of amino acids. He regularly took vitamin and mineral supplements. In fact, he constantly asked his physicians about the contents and affects of his vitamin-mineral supplements. Thiamine and Vitamin B-1 were major components of his vitamin supplements.<sup>2</sup>

According to his physicians, he maintained mental interests and a sense of humor until the end. He carried on business activities while even in a bed-bound state. Movies were a passion and hobby, and he constantly watched them in his living quarters. Some publications have made fun of Hughes' habit of watching movies. His physicians, however, stated that he not only loved movies, but he watched them for technical tips and he even thought about making some movies as he did prior to his plane crash. Daily movie watching as a hobby is a little unusual, but its not any more strange than watching an internet screen all day. Whatever the hobby or activity may be, it's better than having an idle mind and time on one's hands that may depress an intractable pain patient and shorten life.

now many anti-inflammatory agents which pose much less risk to the kidneys and rarely cause peptic ulcers or gastrointestinal bleeding. Interestingly, diazepam is still a highly prescribed drug for intractable pain patients. It is one of the few agents available that provide bonafide muscle relaxation, opioid withdrawal suppression, neuropathic blocking effects, and sleep induction. Dosages, however, are usually below those used by Hughes, because today's pain patient is treated with more effective opioids than codeine, thus eliminating the necessity to use so much of a sedative drug like diazepam.

There are also numerous therapeutic measures available today that were not available to Hughes. Since Hughes' day, magnetic resonance imaging (MRI's) has been developed. Hughes' spine would be evaluated with MRI's today to see if any surgery or other new technologies could eliminate his neck and upper back pain. We now have excellent new neuropathic treatment agents such as duloxetine (Cymbalta<sup>®</sup>) and pregabalin (Lyrica<sup>®</sup>). Electrical stimulators and implanted intrathecal infusion devices are products of modern science and technology, and Hughes would have been a candidate for these measures. The new non-opioid pain

reliever delivered by intrathecal infusion, called ziconotide (Pirlat<sup>®</sup>), might be considered today.

His severe osteoporosis, dental decay, scoliosis, and collapsed vertebrae indicate that adrenal hormone and testosterone testing and replacement would likely be essential. Poorly controlled intractable pain produces hypercortisolemia with resultant osteoporosis, vertebral collapse, and dental erosion.

Apparently, Hughes did not participate in any type of stretching or physical exercise despite his physician's recommendations. The scars from his third degree burns, cervical neck degeneration, multiple nerve injuries, and arthritis were all conditions that respond well to the tailored exercise regimens that are prescribed in modern day pain practices. Surely Hughes would have benefited.

Modern day pain treatment makes great use of topical (applied to skin) medications. The neuropathies that Hughes had as a result of his third degree burns would likely be near the skin surface and would have responded well to topical creams which contain such medications as morphine, carisoprodol, ketoprofen, or ketamine among others. Countless pain patients benefit today from a lidocaine patch (Lidoderm<sup>®</sup>) which provides excellent pain relief for shallow neuropathies.

Routine clinical chemical monitoring of intractable pain patients would need to be done every 6 to 12 months. Patients with a high degree of illness, like Hughes, would require multiple medications and have several concomitant disease processes. For example, routine clinical chemistry would have detected Hughes' impending renal failure and possibly tipped-off doctors to his osteoporosis, hormone deficiencies, and coronary artery disease. Also, today one can assess blood and urine levels of opioids to indicate if the pain reliever has the optimum serum concentration to do the job.<sup>4</sup>

### Lessons Learned

As a long-time practicing physician, the author has several patients with 20-year continuous opioid intractable pain treatment as this article is being written. It is from this perspective the following lessons learned (or maybe lessons we are slow to “learn”) reflect opinions that may have value to the medical community in general.

The major medical lesson for physi-



cians to learn from the Hughes case is to prescribe more potent, long-acting opioids with a short-acting one for pain flares or breakthrough pain and to minimize anti-inflammatory agents and sedatives. There are also some other lessons for IP patients and the major health institutions of today, including professional medical societies, medical schools, government, and health insurance plans. The big lesson is that if Hughes could live 30 years with the poor pain treatment available to him, current IP patients—given modern intractable pain treatment and testing—should easily equal and likely exceed that while maintaining a reasonable quality of life.

The American medical system is primarily structured and organized for care of emergencies, short-term medical problems, and mental disease. It is not prepared with manpower, facilities, or financing for long-term medical problems such as intractable pain, diabetes, and obesity. Intractable pain can only grow in prevalence, since we now have the ability to save people from trauma or disease, and our population is aging.

Another lesson is to quit fighting the use of opioids in whatever dosage is required to treat an individual case. Why? The body's natural endorphins are simply opioids in action, and only opioids can relieve significant pain. Hughes was able to obtain opioids because he needed them to survive. So should anyone else in his predicament. Statements that all severe pain can be treated by non-opioid means are fraudulent. The excuses made by medical persons and institutions to prevent or stop opioid prescribing lack serious thought and analysis. Yes, they may be addicting for street addicts, cause immune or hormone suppression, or hyperalgesia (oversensitivity). No question about it. Just as cancer and heart disease medications cause complications, so do opioids. But what's the option? Leave people shut in at home suffering? What intractable pain patients like Hughes need is an MD who specializes in intractable pain and a clinic system that can provide care and medication for the long haul. Like 30 years or more!

## Summary

Hughes was a flamboyant personality who pushed the envelope in several industries and it is difficult to name a person in the last century who accomplished more. Many of his contributions occurred after 1946 when his plane crashed, he developed intractable pain, and required opioids. Even in his death, Hughes is an inspiration and teacher on how to survive with severe pain and injury. His self-designed, directed, and administered therapeutic regimen should be studied by pain practitioners and patients. The author has attempted to collect as much information and data about Hughes as possible and to be as factual as possible. Even if there are flaws in fact or interpretation, it is clear that Hughes had intractable pain, took opioids, and survived 30 years. The Hughes case calls for identification and study of intractable pain patients who have lived 20 or more years on opioid therapy (see following sidebar). ■

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## CASE REPORTS REQUESTED

This article describes the incredible saga of Howard Hughes as he fought to stay alive for thirty years while clearly suffering intractable pain. This publication has constantly sought approaches to relieve the suffering of these unfortunate individuals and to provide them with adequate lives. We are fortunate to have the authorship of Dr. Forest Tennant who not only played an active role in the post-death analysis of Howard Hughes, but subsequently gained extensive experience as an intractable pain physician and researcher.

*Practical Pain Management* journal poses this question: Are there other, less prominent individuals who managed to survive for twenty years or more? In the interest of learning their secrets we would like any physician with data on a long surviving intractable pain patient to send us case reports for publication. Send case reports to: Dr. Forest Tennant, 338 S. Glendora Ave, West Covina, CA 91790-3043. Fax 626-919-7497. E-mail: veractinc@msn.com.

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