

# Iatrogenic Biliary Injury during Cholecystectomy: Critical Review of a Historical Case and Its Political Consequences

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## Keywords

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## Abstract

Biliary injuries during cholecystectomy represent serious adverse events that can have a profound impact on the patient's quality of life and on the surgeon's well-being and career. Sometimes, they can have an unexpectedly disastrous effect on the whole community, as demonstrated by the case of Anthony Eden, former foreign secretary and prime minister of Britain in the 1950s. Mr. Eden, later Lord Avon, had been suffering from biliary symptoms for a while when he had his cholecystectomy performed on April 12, 1953. On post-op day 1, a bile leak was evident, possibly due to a complete transection of the common bile duct. After a first reoperation to drain a bile collection, the definitive repair was performed in Boston by Dr. Cattell on June 10, 1953, with a loop hepatico-jejunostomy. Unfortunately, the bilioenteric anastomosis became gradually narrow, causing recurrent cholangitis, and Mr. Eden started a symptomatic treatment with pethidine, barbiturate, and amphetamine. These could have affected his perception of

reality and his political judgement during the Suez Canal Crisis and, other than being the ultimate reason for 3,000+ war casualties, might have caused a Third World War. The historical and clinical implications of this case are thoroughly discussed.

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## Introduction

Bile duct injuries represent a fortunately infrequent complication of cholecystectomy. In 1944, Max Simon of the St. Francis Hospital in New York considered cholecystectomy “the most difficult and dangerous of any abdominal surgery” with a mortality rate of about 3% and a high risk of bile duct injuries [1]. Modern data fortunately report an incidence of 0.1% of all cholecystectomies [2], but due to the wide diffusion of this operation, bile duct injuries may be considered a worldwide epidemic with extreme consequences for the patient, the surgeon, and sometimes for the whole community. Their treatment requires high levels of expertise and competence and complex procedures, sometimes leading to liver transplantation. The real incidence of bile duct injuries is probably

still underestimated, and their impact on the society as a whole has not been clarified yet.

In this article we analyse an interesting historical case of iatrogenic bile duct injury that had unthinkable and unforeseeable consequences spreading well beyond the narrow circle of the patient and the surgeon and involving international politics and war. The case of Sir Anthony Eden, former British Foreign Secretary and Prime Minister, presents interesting aspects that have not been clarified yet, despite its international relevance, and is a clear educational example that can be used as a starting point to standardize the modern approach to the treatment of iatrogenic bile duct injuries.

## Case Report

### *First 55 Years*

Robert Anthony Eden was born on June 12, 1897, at Windlestone Hall, in County Durham, North East England, from Sir William and Sybil Frances Eden. Sir William was a landed gentleman with ancient noble blood and family roots going back to the Middle Age as 7th Baronet of West Auckland and 5th Baronet of Maryland (American colonies). Sybil Frances née Grey of Nurthumberland was a locally relevant character with strong family connections with the local conservative circle. The couple had 5 kids, Elfrida Marjorie (1887–1943), John (born in 1888 and killed in action during the First World War in 1914), Timothy Calvert (born in 1893 and deceased in 1963 after inheriting the title of 8th Baronet of West Auckland and 6th Baronet of Maryland), Robert Anthony, and William Nicholas (born in 1900 and killed in action during the First World War in 1916).

Respecting the cliché of aristocratic families, Anthony attended the Sandroyd School in Cobham (Surrey) from 1907 to 1910 and then the Eton College from 1911 to 1915, where it is reported that he excelled in the study of foreign languages. In 1915, he joined the army as second lieutenant at the King's Royal Rifle Corps and in 1916 was transferred to the Western Front, where he earned the Military Cross for saving the life of a soldier. He participated in the Battles of the Somme, Messines, and Ypres and in the Hundred Day Offensive, with the rank of captain. Meantime, Sir William died in 1915 and Anthony inherited a capital of about GBP 380,000 and a yearly income of GBP 35,000.

After the end of the First World War, in October 1919, he entered Oxford University Christ Church College, to perfect his knowledge of oriental languages, and graduated in June 1922 with double first class honour. In July 1920, he was recalled to the Territorial Army (Durham Light Infantry) and had the first episode of epigastric/right upper quadrant pain, diagnosed as “duodenal ulcer.”

After exiting Oxford, in Autumn 1923, Anthony Eden married Beatrice Beckett, daughter of Sir Gervase Beckett, owner of the Yorkshire Post and in November of the same year managed to be elected to the Parliament for the Warwick and Leamington constituency with the minority Conservative Party, and his political activity continued uninterrupted for 34 years. In 1924, the Conservative Party returned to rule the Country and Eden's career had a significant boost. He was appointed Undersecretary for Foreign

Affairs in 1931, Lord Privy Seal in 1933, and, finally, Foreign Secretary in 1935.

During those years that saw the rise of fascism in Europe, Eden met Hitler and Mussolini to try and mitigate their expansionistic politics. Unfortunately, an unpleasant event heavily affected his political influence. In March 1935, he embarked into a political trip all around Europe, visiting Paris, Berlin, Moscow, Warsaw, and Prague. On heading home, his flight was caught in a storm and the plane was so badly shaken that it was diverted to Cologne for an emergency landing. At the arrival, Eden was bradycardic and shocked and remained in hospital in Cologne for several weeks to recover. Upon his return to London, he was seen by the Royal Cardiologist Sir Maurice Cassidy, who prescribed 4 weeks of respite in a nursing home and then 2 weeks of recovery at home. The diagnosis is not perfectly clear, but we can guess he suffered from bradyarrhythmia probably due to vagal hyperstimulation and/or transient ischaemia. For this reason, he was not able to attend the Anglo-French-Italian Conference in Stresa, which was aimed at avoiding the Italian invasion of Abyssinia and the German invasion of Rhineland. The failure of the Stresa Conference led to the wicked “appeasement” of German politics by Sir Neville Chamberlain's British government [3]. Due to his disagreement with Chamberlain upon his appeasement of Hitler and Mussolini politics, possibly justified by an unlucky attempt to keep war and trouble far from Britain and maintain good relations with Hitler's Germany, Eden resigned as Foreign Secretary in 1938 but was reappointed as Secretary of State for Dominions Affairs in 1939 at the onset of the Second World War. Chamberlain resigned in 1940 and the new Prime Minister Winston Churchill wanted Eden as Secretary of State for War and subsequently reappointed him as Foreign Secretary. Eden's outstanding skills for negotiation were extremely useful to Churchill's politics during the reshaping of Europe after the Second World War. In particular he had an active role during and after the February 1945 Yalta Conference, where Roosevelt, already quite ill and probably unable to make sound decisions, supported the expansionistic politics of Stalin without fully involving Churchill in his discussions. Eden participated in all the negotiations with Roosevelt and Stalin and maintained a strict and continuous communication with DeGaulle [4]. In June 1945, final year of WW2, Eden's eldest son Simon Gascoyne was killed in action. This caused a massive shake up of his family's dynamics and Eden's marriage broke down. Eden's personal health suffered too, and he had several episodes of epigastric/right upper quadrant pain. Probably due the previous diagnosis of duodenal ulcer and considering the period of intense stress, he was diagnosed with recurrent peptic ulcer, again in the absence of proper investigations. Later on, in Autumn 1945, he had a biliary colic, treated conservatively. We cannot help thinking that the previous episodes of upper abdominal pain were part of the same problem of gallstones. It could also be not far from truth to speculate that Eden's subsequent right abdominal pain that led to his appendectomy in 1948, performed at the London Clinic by Sir Basil Hume, senior surgeon at St Bartholomew's Hospital, was again due to gallstones. Unfortunately, no record of this procedure is available to us today, but in that period a very high rate of negative appendicectomies was considered to be normal. In 1951, Eden was appointed as foreign secretary for the third time, under the Conservative government again led by Sir Winston Churchill, and on August 14, 1952, he married Clarissa Churchill, niece of the prime minister and Eden's main mentor and supporter.

### *Biliary Problems*

The same year 1952 brought to Eden also recurrent biliary colicky pain, hardly compatible with his intense political activity. For some reasons, his pain was more frequent during long journeys and frequently he had to self-inject pain killers. In June 1952, he also had an episode of jaundice [5]. Between 1 and 5 March 1953, Eden attended a meeting with Eisenhower in Washington, where they were reached by the news of Stalin's stroke. Few days after returning home, Eden met Marshal Tito who was visiting London. At their meeting, Tito commented on Eden's skin to be yellowish in colour. We understand Eden was on what it is known as "colicky status," with continuous biliary pain and jaundice. In fact, as soon as his political commitments allowed him, Eden saw his GP Dr. Rosedale on April 2, when a diagnosis of gallstones was proposed. On the very next day Eden met Sir Horace Evans (personal physician to the King) who confirmed gallstones and possibly common bile duct (CBD) stones. Sir Evans stated that Eden needed a surgical operation and proposed 3 of the most renown British surgeons of that period, namely, Mr. Rodney Maingot (of Royal Free Hospital), Mr. Edward Muir (of King's College) and Mr. (not yet Sir) Edwin Rodney Smith (of St George's). Eden politely rejected the offer and decided to trust Mr. Hume once again, as "Mr. Hume removed my appendix when I was younger, and I'll go to him" [4]. Therefore, on April 4, he had a meeting with Sir Evans and Mr. Basil Hume. They agreed on the diagnosis of stones in the gallbladder and in the CBD and on the need for an operation. The reaction of Winston Churchill was extremely worried, as it can be easily appreciated considering the double link – political and familiar – with Eden, but Dr. Charles Wilson, later Lord Moran, his personal physician, convinced him that Eden would have been safe in Mr. Hume's hands.

Everything was quickly arranged and on April 12, Eden was admitted at the London Clinic to undergo a scheduled operation of cholecystectomy, that was performed by Mr. Basil Hume and Mr. Guy Blackburn (surgeon at Guy's). The day of the operation has been described as a mayhem. On the day, Churchill called Mr. Hume to remark that "nothing should be allowed to go wrong" [6] and specifically requested to be updated in real time on Eden's conditions. Sir Evans became a sort of local representative of 10 Downing Street to the London Clinic, in charge of maintaining an open channel between the hospital and the Prime Minister and sending regular bulletins to Downing Street. Multiple times Evans spoke to Hume to report how anxious Churchill was and to remark the eminence of his patient. As a consequence of this huge pressure, Mr. Hume had a nervous breakdown and the operation was delayed of about 1 h, to give time to Mr. Hume to recover his nerves. Probably this may account for the "over three hours" time Eden spent in the theatre, as noted by Ann Fleming, Clarissa Eden's best friend, in her diary [6].

What happened in theatre is not completely known. Reportedly, the operative notes do not mention anything abnormal, but at the end someone heard Mr. Hume stating that "Eden had two cystic ducts." As likely consequence of this gross misperception, on day 1 Eden was jaundiced, with total bilirubin of 15 mg/dL and had an obvious discharge of bile from the wound. In the absence of interventional radiology or endoscopy, a reoperation was obviously necessary. Eden was informed that during the operation "the knife slipped." Mr. Hume had another nervous breakdown and Mr. Blackburn had to take over Eden's care. It is not clear what impact this had on Mr. Hume's career, but he was anyway already

very close to retirement. After few days when Eden was probably treated with fluids and painkillers, the reoperation was performed on April 29 (post-op day 17) by Mr. Blackburn, who described draining a large biloma and exploring the distal CBD. He did not manage to identify the proximal CBD. The operation was "even more tense than the first" [6] and was concluded after positioning a tube into the distal CBD. In the post-operative period Eden's conditions did not improve much. His temperature was permanently high, and he was jaundiced. The drain did not work much. A percutaneous tube was inserted but did not work either. A new catheter was inserted following the track of the previous drain and a sinogram was obtained. A single image of this investigation was published in a thorough article by Dr. Braasch [7] and it shows a connection between the track and the duodenum. The track going to the duodenum follows the path of the distal CBD, but the irregularity of its walls made them think of a bilioduodenal fistula. The intrahepatic biliary tree can be potentially seen only for a short tract, likely pertaining to the left branches. There is contrast also around the right liver, but it is not clear if there is contrast also within the biliary tree. The most accredited interpretation was that the sinogram showed a complete transection of the proximal CBD with the formation of a bilioduodenal fistula.

Luckily, Dr. Richard Cattell, world-renowned biliary surgeon based at the Lahey Clinic in Boston, was in London for a conference at the Royal College of Surgeons. He was contacted by Sir Horace Evans and summoned to see Eden at the London Clinic. Cattell immediately understood the gravity of the situation and offered a biliary reconstruction to be performed in Boston. He was adamant that he could not guarantee optimal results if not in his own environment and with his highly trained staff. Obviously, transporting Eden to the US was not an easy and cheap undertaking, due to Eden's acute clinical conditions and logistic issues. Moreover, Churchill was not particularly happy to transfer Eden to Boston also for political reasons; in fact, it would be a severe blow to the newborn NHS (set up by Aneurin Bevan only 5 years before) and would be bad publicity for the Conservative Government. After all, said Churchill, King George VI had been "operated on a kitchen table in Buckingham Palace" [6]. Of note, Churchill himself suffered with gallstones and, although he had at least 2 episodes of cholangitis, he was never operated. Eden agreed to the transfer, as he did "not consider that medicine or the arts have national frontiers" [5]. The financial issues were resolved by Lord Woolton, chair of the Conservative Party, who decided to use party funds to cover the transport expenses. Reportedly, the political issues were resolved by the newly coronated Queen Elizabeth II (her coronation took place on June 2, 1953), who made the royal yacht *Britannia* available to Mr. Eden so he could stay on British soil while recovering after being discharged from the hospital. However, no evidence is available to support this thesis.

After a short period of respite at Chequers (the country house of the British Prime Ministers in Buckinghamshire), Mr. and Mrs. Eden flew to Boston just after Elizabeth II's coronation, on a comfortable plane fitted with a bed, sent by the Governor General of Canada, and were greeted by Eden's son in Boston. The British ambassador and former member of Eden's staff Sir Roger Makins organized Eden's stay in Boston and spoke with Dr. Cattell, who informed him that Eden had a risk of intraoperative mortality of about 50% and a possibility to heal completely of about 10%.

The operation was performed by Dr. Richard Cattell and Dr. John Braasch on June 10, 1953, at the New England Baptist Hos-

pital in Boston. The surgeons described a bilio-duodenal fistula, a very short segment of proximal common hepatic duct and a globally enlarged liver. The fistula was taken down, the spur of the confluence was divided, and a loop hepatico-jejunostomy on a 16Fr Y-tube was fashioned and completed with an enteroenterostomy at the basis of the loop [7]. Eden's postoperative recovery was uneventful. After discharge, he remained few days on the Britannia and then moved to Jamaica to stay in Ian Fleming's property Goldeneye. Ian Fleming, writer of the James Bond 007 character and himself a naval intelligence officer, was Ann Fleming's husband and good friend of Clarissa and Anthony. His Jamaican house was named after a WW2 US-UK plan to monitor Spain for possible alliances with Hitler and Mussolini and gave name to one of Bond's adventures. During Eden's recovery in Jamaica, Prime Minister Winston Churchill had one of his recurrent strokes, with temporary paralysis. The natural successor in his role of PM was Anthony Eden, but he was still recovering out of the country, so Churchill's illness was kept secret until Eden was able to come back to the UK.

In 1954, Eden was created Knight of the Garter, but on the same year he had an episode of cholangitis, treated conservatively. On April 6, 1955, he was appointed as Prime Minister, after Churchill's resignation. During the same year, and the year after, he had several recurrent episodes of cholangitis with fever up to 41°C. His pretty much constant illness, associated with the stress and lack of sleep of his office in that delicate international political contingency, heavily impacted on Eden's mood.

He was also in constant pain [8] and was prescribed heavy painkillers (pethidine) and sleeping tablets (barbiturate). As a consequence, he had to rely on the effects of amphetamines to counteract the effect of the former. Specifically, he was on Demerol (pethidine), Seconal (secobarbital), Drinamyl – also known as “purple hearts” – (amphetamine and amobarbital) and Benzedrine (D- and L-amphetamine). Churchill himself was on Seconal and Drinamyl, prescribed by his personal physician Lord Moran [8–10].

#### *Suez Crisis*

The idea of setting up a communication between the Red Sea and the Mediterranean dates back to the Pharaoh Senusret 3rd but was achieved only by Napoleon in the 19th Century. The planning for the Suez Canal was initiated in 1854 under the guide of the architect Ferdinand De Lesseps who agreed to form the Suez Canal Co. with the Egyptian viceroy. Initially, the British government opposed the canal as it was considered a way to favour French business over British global shipping, but in 1875 the British government took over 44% stake of the company from Egypt. The canal was finally opened on November 17, 1869, under the ownership of the company and the protection of the French and, later, the British. It has always been considered to be crucial for the British economy, as well as the rest of the European countries, as it shortens by 5,000 miles the distance between India and London. In 1954, about two-thirds of oil supply in Europe was coming through the canal. On June 13, 1956, the last British troop left the Suez area that had to be returned to Egypt as per previous agreement, but on July 26, 1956, Gamal Abdel Nasser, president of Egypt, assumed control of the Suez Canal and froze all the assets of the Suez Canal Co.

The news of the “nationalization” reached Eden when he was at dinner with King Faisal of Iraq at 10 Downing Street. His initial response was quite prudent, in line with his usual attitude of negotiation and accurate planning, but soon his behaviour changed significantly. The effect of massive doses of psychoactive drugs prob-

ably reflected on Eden's mood at n.10 [8] and on his perception of the political situation. On 27 July, he had a meeting at n.10 with the US and French ambassadors, 4 ministers of his Cabinet, and 2 chiefs of staff. The accepted option, endorsed by the retired Churchill, was to bomb the canal and surrounding villages using 3 armoured divisions and from there progress to seize Cairo to overthrow Nasser and his government. There were at least 3 different orders of reasons for Eden's aggressive response: (a) international reasons – while it was perfectly within Nasser's right to take over the canal, according to the Suez Canal Base Agreement, the use of force and mostly the nationalization of the assets of the Suez Canal Co. were considered to be excessive; (b) national reasons – UK reserve of oil were sufficient for only 6 weeks and >50% of oil supply to the UK came from the canal; (c) personal reasons – Eden was obsessed by Nasser, whom he called “the new Mussolini” [6]. UK Foreign Secretary, Anthony Nutting, suggested prudence and claimed that US should have been involved in any decision, but Eden replied with such vehemence that Nutting probably felt threatened and resigned.

Negotiation continued for the whole summer, and in October 1956 a secret protocol was signed in Sevres (one of the suburbs of Paris) by England (Eden), France (Mollet), and Israel (Ben Gurion) to attack Egypt and regain control on the Suez Canal. Israel attacked Egypt on October 26 at 3 p.m. and gained control on the Sinai Peninsula. Egyptian counterattack with the navy was easily rejected. On the very next day, England and France sent an ultimatum to both Egypt and Israel to withdraw, but this had been clearly prearranged with Israel to justify the Anglo-French attack to Suez. On the 29th, English and French troops started bombing the canal and surrounding villages, including Egyptian troops, with the false pretence to separate Egyptians from Israelis. On November 2, the General Assembly of the United Nations called for ceasefire, with no response from the Anglo-French coalition. On November 5, the canal fell on English and French hands. A second ceasefire was sent by the UN on November 6. This came along with huge political and diplomatic pressures. At home, Eden was heavily criticized by political opponents but also from the same Conservative Party so that he became effectively isolated within the Cabinet, with only 3 ministers actually supporting his decision, mostly with imperialistic reasons, to try and maintain the historic influence of Britain in the Middle East. Abroad, US threatened to withdraw their political and financial support – it is worth clarifying that Suez did not represent an important pathway for the US, as only 15% of their oil came from that route – so welcome and crucial after the end of WW2. Furthermore, in the months before the “nationalization,” Nasser was leaning towards the influence of USSR and gained the strong support of Khrushchev (First Secretary of the Communist Party) and Bulganin (Prime Minister). As a consequence of the Anglo-French attack on Suez, Khrushchev threatened rocket attacks on London, Paris, and Tel Aviv, opening de facto the way to a Third World War. Meantime, on October 24, the Hungarian Revolution started, adding political fibrillation to the already messed up European situation, and was nipped in the bud by the Red Army on November 11. Hardly we could believe that this international complication did not put further pressures on Eden and his government. On November 23, the British and French troops began to withdraw, and the recall was completed by December 22. Eden had to bow to internal and external pressures but did not renounce his plan to kill Nasser. Quite expectedly, all the MI6 agents in Egypt had already been rounded up by the Egyp-

tian forces at the onset of the war. Eden tried to use renegade Egyptian officers, but their action failed due to lack of weapons [11].

The Suez War ended therefore on November 23, 1956, leaving >3,000 casualties. The British Army had 16 deaths and 96 wounded soldiers. The French troops had 10 deaths and 33 wounded. 231 Israeli soldiers died and about 900 were wounded. The Egyptian Army had >1,000 deaths and an unsure number of wounded. One of the men responsible for his mayhem was undoubtedly Anthony Eden, whose physical health was heavily affected by recurrent episodes of cholangitis and whose mental health was impaired by the amphetamines and barbiturates he was on.

Sir Horace Evans clearly stated that:

His general health during the past year has been maintained with extensive vitamin therapy – sodium amytal gr 3 and Seconal en-seal gr 1.5 every night and often a tablet of Drinamyl every morning. These treatments have only become really essential during the past 6 months. Before his rest in Jamaica, the general condition was one of extreme overstrain with general physical nerve exhaustion, and at this time he seemed to be helped by rest, some increase in the sedation and vitamin B12 therapy. [8]

Eden himself noted in his diary:

consulted Dr. Evans or Dr. Kling on at least 10 occasions between the canal nationalisation and the end of October [8].

On October 5, Eden had a severe episode of fever up to 41° and rigours, that lasted >24 h and had to increase the dose of psychoactive medications. As a consequence, Lord Evans suggested a respite period and Eden decided to fly to Jamaica on November 23, feeling that Fleming's Goldeneye was the only place where he could regain a bit of health.

As a consequence of his untoward decisions during the crisis, quite inconsistent with his usual prudent and negotiation-prone attitude, Eden was isolated in the Cabinet and was derided at the Commons upon his return. US withdrew its political and economic support, causing a significant fall of the value and purchasing power of the British pound. Meantime, Western diplomacy had to frantically try to reduce USSR menace to bomb European cities. This led to Eden's resignation as Prime Minister on January 9, 1957. At the same time, he also resigned from the Commons.

Clearly, during the Suez Crisis, Eden made a series of terrible misjudgements. According to the Canal Base Agreement, the canal had to be returned to Egypt anyway, therefore the use of force was considered to be an unduly aggression. This was made clear by Sir Reginald Manningham-Buller, Attorney General, but Eden did not consider his expert opinion.

England and France had no right to change the Egyptian regime and, mostly, to overthrow and kill Nasser. This would not have been acceptable by the UN Security Council and by UK's strongest supporters (US).

Eden did not consult Eisenhower before acting. This was not acceptable by the US President, especially during the week of US general elections.

Eden misread the American attitude towards his politics, thinking that Eisenhower would support his choice to attack Egypt. On the contrary, the US President and government were against any war action, in particular if suspected of colonialism.

Eden, Mollet, and Ben Gurion did not consider that USSR strongly supported Nasser and was bound to intervene should the Suez war progress. This might have led to a Third World War.

Eden lied overtly to the Commons regarding his intention to collude with Israel and France. He denied any knowledge that Israel would invade Egypt, whereas the secret protocol of Sevres, known to the entire Cabinet, stated the opposite.

According to most of the historians, Eden's political failure and consequent resignation had their roots in his illness and consequent pharmacological treatment. Eden's physicians clearly stated that his poor health would not be consistent with his political commitments [12] and their report was made known to the queen, who accepted Eden's resignation on the basis of his illness. During the Suez Crisis, Eden's symptoms of recurrent "cholangitis" progressively worsened and he had to increase significantly the dose of amphetamines and barbiturates. This was made clear to the Cabinet in Eden's resignation speech on January 9, 1957, as reported by Lord Owen [8].

#### *Further Biliary Problems*

Due to recurrent episodes of fever with rigours – and normal liver function tests – Eden was readmitted to the New England Baptist Hospital, Boston, on April 7, 1957. Even if his blood tests were all normal, the bromsulphalein test showed 15% retention (normal value <5–10%), thus demonstrating a degree of biliary obstruction.

On April 13, he underwent his operation n.4. At relaparotomy Dr. Cattell described a normal liver, but a stricture of the biliary anastomosis, whose size was about 7 mm. There was also a stricture of the right hepatic duct with a diameter of 2 mm. There was no trace of the Y-stent that was inserted at the first operation. Both strictures were dilated through a jejunotomy and a liver biopsy was performed. Histology did not show any evidence of cholangitis or biliary stasis.

After few years of good health, Eden suffered from recurrent cholangitis from 1960 to 1969. Blood tests were always normal, other than a single episode in 1969 when alkaline phosphatase was raised. A Barium meal in 1965, reported by Braasch [7], showed a patent anastomosis with left lobe hypertrophy. Another Barium meal in 1969 confirmed the patency of the anastomosis but failed to visualize the right anterior segment.

Meantime, in 1961 Eden was created Earl of Avon and entered the House of Lords. In 1962 he had another operation of excision of a benign chest wall tumour. This was performed at the Lahey Clinic in Boston. Unfortunately, we do not have any evidence or further information of this operation, reported by Braasch [7]. However, it sounds quite odd that Eden decided to fly to Boston to have what looks like a simple procedure.

Operation n.5 was performed on March 5, 1970. Dr. Cattell having passed away on September 18, 1964, the operation was performed by Dr. Braasch. He found a small right lobe and a compensatory hypertrophy of the left lobe of the liver. The left biliary duct was normal, but there was a stricture of the right duct. After accessing the jejunal lumen, Braasch dilated the right duct stricture, inserted a cannula into the right duct and performed a cholangiogram. This showed a "cavity" within the right anterior segment of the liver (segments 5–8), with an extensive extravasation of contrast within the liver parenchyma. He then decided to insert a 12 Fr rubber tube from the jejunum to the skin through the right duct and the liver parenchyma. Unfortunately, this percutaneous biliary drain came off 3 months after the operation [7].

Postoperative recovery was uneventful. After this operation, Eden had a long asymptomatic period from 1970 to 1975, but had

another episode of fever with shivering in 1975. A Barium cholangiogram came back as normal. On the same year he was diagnosed with prostatic cancer and medical treatment was started. Due to recurrent fever up to 38°C, Eden was admitted again in 1976. Alkaline phosphatase was raised but the other blood tests were normal. A scan showed multiple bone metastases and enlarged mediastinal lymph nodes.

On January 14, 1977, Eden died in Salisbury, aged 79, and was buried in St Mary Churchyard at Alvediston. The title of Lord Avon was passed to his only surviving son, Nicholas, who was also a politician and the youngest Minister in the Government of Margaret Thatcher. His political activity was also affected by his poor health until he died of AIDS in 1985, aged 54.

It is not completely clear what was the ultimate cause of death of Anthony Eden. The most accredited view is that he died of “liver cancer” [13], but other hypotheses have been raised, such as “metastatic prostatic cancer.” In his obituary, the Times stated that “Eden was the last Prime Minister to believe Britain was a great power and the first to confront a crisis which proved she was not.”

## Discussion

At a first glance, Eden’s case looks paradigmatic of an iatrogenic biliary injury with unfavourable outcome. However, it is possible to do some considerations and raise some doubts.

### *Biliary Lesion*

Prevalence of biliary injury during cholecystectomy has gradually reduced with time. From 1858, when Bakes reported postoperative bile leak in 230 out of 246 cholecystectomies [1], today the incidence of iatrogenic biliary injury is reported in 0.1% of cases [2]. Already in 1981, in their relation to the 83rd Congress of the Association Française de Chirurgie, Bismuth and Lazorthes reported a risk of CBD injury of 1–2 cases out of 1,000 cholecystectomies and this was strictly dependent on the experience of the operator, being 0.34% in series with <500 cholecystectomies and 0.08% in those with >1,500 cholecystectomies [14]. We wonder, however, if this estimate is fully reliable. In fact, the very most of epidemiological studies on iatrogenic CBD injuries come from high volume tertiary centre and may be based on the number of cases referred to them. On the contrary, a large number of bile leaks are nowadays treated by endoscopic or percutaneous approach in the hospital where the injury happened and the surgeon who had the complication may not be totally happy to publish his/her own failures.

Unfortunately, in 1952, when Eden had his cholecystectomy, the risk of biliary leak was still extraordinary high. In 1949, Thorlakson reported that, of patients sustaining injury of the bile duct during surgery, one third

died soon after the operation, one third died as a consequence of the attempted repair and the remaining third, who had good results from the secondary operation, had their life marked by recurrent attacks of pain, jaundice and fever (i.e., cholangitis) [15].

It has been proposed that the most probable mechanism of lesion is the so-called “tenting” of the CBD, where the Hartmann’s pouch is excessively pulled laterally and anteriorly and the CBD is “tenting” towards the right side. This may be consistent with the reported statement that “Eden had two cystic ducts.” In fact, the probability of duplication of the cystic duct is extremely low [16]. According to Kune, the distal ligature could have been on the cystic duct, but the proximal one was on the CHD. The subsequent division removed a segment of CBD and left the proximal stump closed. The tie could have just slid out within 24 h, probably due to the increased pressure within the bile tree. This may explain why Eden had a subhepatic bile collection and Mr. Blackburn was not able to find the proximal biliary stump during the second operation.

It is not clear if Mr. Hume left a subhepatic drain after the operation. Although we could consider quite unlikely that an experienced surgeon in the ‘50s completed an open cholecystectomy on the Foreign Secretary without protecting the patient – and himself – with a subhepatic drain, the fact that Eden developed a subhepatic bile collection raises the possibility that he did not.

The fact that the biliary confluence has been spared is also demonstrated by the fact that the first biliary repair performed by Dr. Cattell was an hepatico-jejunostomy at the biliary confluence, with division of the spur of the confluence. We can speculate that the initial tie was already quite high but the ischaemic injury of the biliary tissue by the tie could have reduced further the segment of CHD available for the repair, as if an initial lesion Bismuth type 2 or Strasberg type E2 transformed into a Bismuth type 3 or Strasberg type E3, that is, at the floor of the biliary confluence. However, we feel that the mechanism of lesion might be completely different. In fact, it is our experience how a “tenting” lesion happens usually in patients with non-inflamed gallbladders (no retraction on the gallbladder pedicle), where the CBD is abnormally long and mobile, which probably was not Eden’s case. In fact, Eden had been suffering of recurrent biliary pain for a while and we would expect a degree of chronic inflammation with retraction of the gallbladder pedicle. Possibly, he might have had a scleroatrophic gallbladder with stones also in the common duct. In these conditions, a “tenting” mechanism looks quite unlikely.

The sinogram performed on May 16, 1953, 1 month after the operation, is not completely clear. At that time it was interpreted as showing a bilio-duodenal fistula and minimal opacification of the intrahepatic biliary tree. Actually, it does not seem to show any contrast within the extrahepatic CBD. There is probably some contrast in the duodenal lumen. The intrahepatic ducts are not clearly identified – possibly only the ducts to segments 2, 3 and 4 of the left hemiliver are visible – and there is some leak of contrast in the subhepatic space.

Prof. Kune proposed that a vascular lesion was associated with the biliary injury. Likely, it was the right branch of the hepatic artery to be involved in what looks like a Strasberg E3 lesion [4]. The reasons why he raises these hypotheses are: (a) the CHD is strictly associated with the right hepatic artery, (b) hypotrophy of the right lobe of the liver, with compensatory hypertrophy of the left lobe, was demonstrated later on in Eden's course, (c) a stricture of the right hepatic duct quite far from the anastomosis, therefore probably of ischaemic aetiology, was found at 2 operations in Boston, and dilated [4]. However, if there was a truly ischaemic lesion, an hypotrophic right hemiliver would have been evident already at the first repair performed by Cattell. We tend to favour the hypothesis of a progressive secondary biliary cirrhosis of the right hemiliver due to the right duct stricture.

The mechanism of injury has never been confirmed. In actual facts, it is not even clear what kind of operation Eden had on the April 12, 1953. It is commonly believed that he had a simple cholecystectomy, but it is also possible that he had some form of biliary duct exploration, if we want to take as granted Marshal Tito's remarks on Eden's jaundice. However, the fact that he was operated almost 1 month after that episode of jaundice makes us think that his jaundice was not progressive but, on the contrary, subsided spontaneously, as if a stone passed through the duct and was expelled.

Blaming anatomical abnormalities for every surgical complication is an old self-defensive mechanism, well known in every operating theatre [17]. Iatrogenic CBD injuries are usually linked to anatomical misidentification of the landmarks [14, 18] due to ambiguous inputs received from "signals" (obvious anatomical structures) and "noise" (inflammatory tissue, blood, fat tissue, adhesions) [19]. The central error in this case is usually a wrong mental image that convinces the surgeon that the CHD is a duplicated cystic duct. An associate mechanism can be the underestimation of the surgical risk typical of experienced surgeons who base their overconfidence on their positive past record [20].

On the basis of these considerations and of the statistics on CBD injury, we may guess that if Eden had chosen one of the surgeons proposed by Sir Evans (Rodney Maingot, Edward Muir or Edwin Rodney Smith) his actual risk of CBD injury may not have been reduced. However, other human factors – specific to Hume – played a role in the surgical complication. Before the operation, Mr. Hume was under an extraordinary pressure mostly by Winston Churchill and his entourage and had a nervous breakdown. Although he had about 1 h to recover and shared the burden of this operation with another experienced surgeon, Mr. Blackburn, we can be authorized to guess that his surgical judgement was at least mildly impaired, therefore the hypothesis of a misperception is highly likely. In fact, in situation of stress, although senses can be enhanced due to the high level of "stress hormones," we tend to rely on preconceived images which do not necessarily correspond to truth and to overimpose our mental image on the visual inputs coming from the surgical field (or the monitor in case of endoscopic surgery). This phenomenon of misperception has been widely described by the Italian psychologist Gaetano Kanizsa in 1955 [21]. The impact of Mr. Hume's character on the genesis of this complication has been analysed elsewhere [17].

#### *Operation n.2: Drain*

It is not perfectly clear why the reoperation was delayed for several days if the biliary fistula was diagnosed on POD1. We can guess that political pressure had an important role. Moreover, common experience and psychology show that often the first reaction of the surgeon involved in a surgical complication is of denial [17]. This may well be the case with Mr. Hume, who is known to have had a second nervous breakdown as soon as the complication became evident, so that Mr. Blackburn had to take over the care of the illustrious patient.

Furthermore, it is not clear if Mr. Eden had any kind of investigation before the reoperation. Considering that CT and US scan were not available in 1953, we guess that the operative indication was only based on the physical signs and clinical presentation. Also, it is not clear what kind of treatment Eden had for his postoperative sepsis. Actually, it is not fully demonstrated that he had sepsis, but we can reasonably think he was septic as he had fever and a bile collection. The sudden rise of total bilirubin of 10-folds the normal range would raise the suspicion that Eden had a complete closure of the CBD at the first operation, but it has been mentioned that he became quickly septic and there was bile discharge from the wound already in day 1. We therefore guess that he might have

had a complex biliary injury with stricture/ligation and leak.

During the second operation, a large biloma was drained but apparently no subhepatic drain was left. We know that the distal CBD was explored and possibly intubated, but Mr. Blackburn could not identify the proximal stump. Braasch described that Mr. Blackburn left a T-tube in the distal stump. We find hard to understand how this would be possible in the absence of a clear proximal stump to receive the proximal segment of the T-tube. Again, it is not clear if Mr. Blackburn left a subhepatic drain. According to Braasch, probably he did not [7]. The question of the presence or not of a subhepatic drain at the end of the first two operations is of great importance. Although, as previously stated, we consider unlikely that two experienced surgeons did not drain the subhepatic space after two complex operations, evidence seems to point towards this possibility. However, a commonly used drain in the 50s was the Penrose drain, that is essentially like a glove finger with a gauze inside, where fluids are drained by capillarity. Although this may be useful to drain a minimal discharge, it would have been totally unfit to drain a big subhepatic collection. On the contrary, it is crucial that the subhepatic space is thoroughly drained possibly with multiple large-bore drains. In fact, the subhepatic biloma under tension created a spontaneous fistula with the superior aspect of the duodenum which, in those inflammatory conditions, tends to get stuck to the inferior surface of the liver and the gallbladder bed. Best practice would have suggested a thorough and aggressive drainage with multiple large-bore tubes. Our experience is that rubber tubes, instead of silicon ones, are preferable as they create dense local adhesions and favour the formation of a fistula that avoids bile leaks in the peritoneal cavity once the drain is withdrawn. A slow withdraw of the drain would “guide” externally the fistula, thus allowing a progressive and “clean” stricture of the bile duct.

We can guess that the operation was particularly difficult, not just for the objective difficulties of an abdominal reoperation 2 weeks after the first one, that is, in the moment when adhesions are more florid, and on a septic patient, but also for the surrounding political pressure. It is common experience that the first reoperation for a postoperative biliary fistula is usually performed by the same team that caused the injury, who may not have the specific expertise to repair a biliary injury. It's been widely demonstrated that the best results of biliary repairs are obtained in tertiary biliary centres with a multidisciplinary approach and most of authors now suggest that

the repair should not be attempted by the surgeon who had the complication [22–24]. We have always suggested that the first reoperation should only entail a washout and drain, without any attempt at repairing the injury. In fact, in those conditions, even if the anatomical structures are identified – which is not guaranteed – “a common bile duct soaked in bile has the same consistence of a wet Cleenex” (Bismuth H., unpublished citation) and every suture is bound to fail. Moreover, any attempt of biliary suture would have reduced the already minimal available biliary tissue and would have made the subsequent operation by Cattell extremely tricky. Classical teaching and good practice would suggest that every biliary reconstruction must be delayed until the formation of a biliary stricture, but on the other hand, an early reoperation was absolutely indicated, due to the presence of an open fistula and sepsis and very well did Mr. Blackburn not to attempt any repair.

A successful biliary repair would need 4 separate phases:

- 1 Treat the biliary peritonitis and sepsis
- 2 Control the biliary fistula
- 3 Await until the fistula dries up and bile duct dilates
- 4 Perform a correct bilioenteric anastomosis

Mr. Blackburn reoperation probably fulfilled the first step, but likely did not manage to guide the biliary fistula and the lack of a subhepatic drain delayed the postoperative recovery.

We understand that Eden, his wife and mostly his mentor PM Winston Churchill were anxious to obtain a prompt and definitive recovery. Through political and academic channels, Dr. Cattell was summoned to give his opinion. From the description of the operations and the clinical conditions of the patient, Cattell understood that a biliary repair was necessary and managed to get Mr. Eden to Boston.

We speculate that before flying to Boston, Eden must have recovered a sufficient degree of health to allow him and his wife to participate to Queen Elizabeth II coronation on June 2, 1953. The presence of a working subhepatic drain might have allowed the external fistula to establish and mature, thus reducing the local septic component, but there is no evidence that the tube actually worked long. Another more interesting option would be that a spontaneous bilioenteric fistula established, thus allowing a good passage of bile and the recovery of the patient. However, if we take for granted the hypothesis of a Strasberg E3 lesion with complete division of the CHD, the closure of the fistula would only mean the complete closure of the proximal stump, but in that case



the patient would have been deeply jaundiced, which likely is not the case as Eden attended formal commitments before flying to Boston and nobody mentioned any jaundice or, worst, ongoing cholangitis/sepsis. On the contrary, the fact that Eden recovered pretty well before going to Boston, can be explained with the formation of a bilioduodenal fistula.

### *Operation n.3: Biliary Repair*

There is no doubt that the operation Dr. Cattell performed on Mr. Eden in Boston was the best the surgical world could offer at that time. Nowadays we would have preferred a Roux-en-Y hepaticojejunostomy, to reduce the risk of food contamination on the bilioenteric anastomosis, but the division of the spur of the confluence Cattell performed is a demonstration that the anastomosis has been correctly performed on the proximal hepatic duct, where the risk of stricture is lower as the bile duct is wider, well supplied and far from the chronic inflammation. Moreover, if we trust the anonymous knight-surgeon that wrote to Cattell saying that Eden's fistula had dried up when he left England to be admitted to the New England Baptist Hospital, it is possible that the proximal duct was already quite dilated due to the distal stricture.

As a matter of fact, the timing for the repair was about 2 months, which is the recommended waiting for a biliary repair, as the inflammation had been treated, the biliary lesion was stabilized, in terms of no further ischaemic injury on the biliary mucosa, the biliary walls were probably thick and healthy and the proximal stump was dilated. This is what we would expect had happened in Eden's case, but there is no reliable evidence that this actually happened.

Technically speaking, it is undoubtful that Cattell performed an operation well ahead of times. In fact, Hepp's revolutionary article on biliary reconstruction would have appeared only 3 years later [25] and Smith's mucosal graft technique would have been published only in 1975 [26]. In 1953, the Longmire's operation (left lobectomy and hepatojejunal anastomosis) [27] had already been abandoned and the reference operation was Cattell's loop hepatico-jejunostomy performed at the biliary confluence after division of the spur and stented with a Y-tube. Although there is no evidence that Cattell performed what we nowadays consider as a crucial step in hepatico-jejunostomy, that is the manoeuvre of lowering the hilar plate so that a good access to the biliary confluence can be obtained, we are sure that the anastomosis was performed according to best practice and there was no postoperative leak. However, good health did not last long, and even

before his appointment as PM, in 1954 Eden had an episode of cholangitis. Since then, he had several other similar episodes – at least 3 in 1955 and multiple episodes in 1956. It is possible that in Eden's case the sense of duty prevailed over his own illness and he decided to accept the post of PM offered by his Party, despite his recurrent illness, but it is also possible that his own character and will to climb the stairs to power overcame his own symptoms.

Eden's episodes of illness that followed his biliary repair have been always labelled as "cholangitis." The Charcot's definition of cholangitis is of a clinical syndrome of jaundice, pain and fever with rigours. The Reynold's pentad includes also low blood pressure and mental status changes. Although Eden might have had pain and fever with rigours, and possibly low blood pressure and also decreased level of consciousness [5], he has never been jaundiced and his liver function test have been always normal. We know he had pain, as he was on regular pethidine, and that he had fever up to 41° and rigour. We know also that he had episodes of low blood pressure that did not allow him to attend important meetings during and after the Suez Crisis. We wonder why he did not have any jaundice and his blood tests were usually normal.

Critical strictures of hepaticojejunostomies are usually associated with jaundice and dilatation of the intrahepatic ducts. As there is no reason not to trust Braasch's and Cattell's operative notes describing the presence of a stricture of the right hepatic duct, Eden could have been suffering of cholangitis of the right hemiliver, with a normally functioning hypertrophic left lobe. Although this can justify the absence of jaundice, there is no evidence of biliary obstruction in the right liver. In fact, other than the normal liver function tests, the barium cholangiograms performed in 1965 and 1969 did not show any biliary dilatation but only a hypotrophic right lobe. Both these cholangiograms did not show the right anterior (paramedian) segment, so it could be possible that the intrahepatic stricture was only of the right anterior duct, not involving the main right duct.

At a more accurate survey, we have the impression that both 1965 and 1969 cholangiograms may not show any duct of the right hemiliver. Although the duct seen on the right side can well be the duct for segment 6 (in ideal continuation with the duct for segment 2), it could well be a left paramedian duct completely displaced on the right side by the huge dilatation of the left hemiliver. In case of right duct stricture and subsequent hypotrophy of the right hemiliver, the hypertrophy of the left hemiliver would rotate the liver axis and the liver pedicle counter-clockwise to the right side, making the ducts for segment

4 appear on the right side of the cholangiogram. On the contrary, if there was a stricture of an isolated segmental duct, we would not expect a significant hypertrophy and rotation of the left hemiliver, and those cholangiograms would show a normal posterolateral duct. However, if this was the case, we would hardly believe that an isolated stricture of a segmental bile duct could create so many debilitating episodes of acute cholangitis. It is also possible that the original lesion was not on the CHD, but on an abnormal right anterior duct slided down on the CHD. This duct probably closed completely due to scar retraction and chronic inflammation; therefore, it is not visible at the barium cholangiogram.

Multiple recurrent cholangitis is a not-so-rare complication after biliary repair with hepatico-jejunostomy. Should we be able to apply the modern metrics of the Cho's classification, the results of Eden's repair could be classified as Cho Grade C [28]. It is well known that the vast majority of re-stricture happen within the first year [28], and Eden's case was not an exception, as the first episodes of cholangitis was within a year from the operation. Primary patency was achieved but was lost very soon due to re-stricture. Another contributing factor may be that the enteroenteric side-to-side anastomosis at the bottom of the loop bilioenteric anastomosis was too close to the biliary tree – as demonstrated by the barium cholangiograms performed in the 60s – therefore increasing the risk of retrograde cholangitis.

#### *Operation n.4: Dilatation of Biliary Strictures*

Operation n.4 was necessary due to Eden's recurrent "cholangitis." Clearly, at that time non-conventional radiology was moving its first steps and advanced diagnostic and therapeutic modalities were not yet available. When Eden was admitted to the New England Baptist Hospital in Boston on April 7, 1957, his blood tests were normal and the only mildly abnormal investigation was the bromsulphalein clearance test, showing 15% retention, against a normal rate of <10% after 30 min and <5% after 1 h from the injection of 5 mg/kg of bromsulphalein. Eden was offered a surgical exploration only on the basis of a positive bromsulphalein test. Unfortunately, the diagnosis of biliary stricture was done at the surgical table. The main stricture was at the anastomosis, whose lumen was 7 mm wide, most definitely not enough to guarantee a good bile flow. However, the fact that probably Eden was not jaundiced when he had his biliary repair makes us think that probably his CHD was not too dilated, therefore the bilioenteric anastomosis was more prone to stenosis.

A bit more difficult is to explain the finding of a stricture of the right hepatic duct. It has been advocated that this was an ischaemic stricture due to arterial injury and consequent ligation of the right hepatic artery during the cholecystectomy. This mechanism may also explain the occurrence of the stricture of the bilioenteric anastomosis. However, although both the right duct and the right part of the confluence are supplied by arterial branches coming from the right hepatic artery, it is known that an anastomotic branch running below the hilar plate and a microscopic vascular network connects the right and left arterial systems just in front of the confluence, making an ischaemic lesion less likely [29]. Furthermore, as previously mentioned, an ischaemic injury would have caused right lobe hypotrophy much sooner and Cattell would have mentioned it in his operative notes. The surgical choice of a simple dilatation of the strictures through a jejunotomy is hardly justifiable with the modern knowledge. Nowadays we would have probably preferred endoscopic or radiological gradual calibration and multiple stenting, possibly via a percutaneous approach, or re-anastomosis. Slow calibration is much better than forced dilatation as the latter causes an important mucosal trauma with further scar tissue and re-stricture. However, we appreciate that in 1957 the chosen operation would have been considered the safest approach. For sure, if the proximal biliary stricture had to be removed, the necessary operation would have been either a multiple cholangioenterostomy (on the right segmental ducts plus the left duct) or a right hepatectomy followed by left cholangio-jejunostomy. These would probably be more effective options, but at that time Cattell and Braasch opted for the less invasive option. After the operation, Eden enjoyed 3 symptom-free years, but then from 1960 to 1969 he experienced recurrent cholangitis. Two barium cholangiograms performed in 1965 and 1969 showed a patent anastomosis, no intrahepatic dilatation and hypertrophy of the left hemiliver. The right anterior segment was never visualized. Actually, as mentioned before, we are still very doubtful that the posterolateral segment was visualized, either.

As mentioned before, we can hardly justify recurrent cholangitis with the reported radiographic pictures of no biliary obstruction. We wonder if Eden's cholangitis was mostly due to intrahepatic proximal stones intermittently obstructing an otherwise patent anastomosis. However, a more prudent interpretation of the two retrograde barium cholangiograms may show a different picture. At a first glance, the cholangiogram shows a significantly hypertrophic left liver. The small opacified duct on the right

seems to be the duct for segment 6, in virtual line with the duct of segment 2, but this would be the case in a “normal” liver. In Eden’s case, the hypertrophy of the left hemiliver would have caused an anticlockwise rotation of the hepatic pedicle, so that the hypotrophic right hemiliver was moved backwards and the left hemiliver became anterior. The ducts erroneously attributed to the right hemiliver could in fact represent the biliary ducts of segment 4. If our hypothesis is true, the initial biliary injury would have been a Strasberg 5 lesion of an abnormally positioned right anterior duct, which closed very early. The subsequent bilioenteric anastomosis was very wide on the left duct, as it happens usually, but narrow on the right duct, which in actual facts would be the right lateral duct. The latter underwent a progressive stricture that, associated with the already established stricture of the right anterior duct, would have caused a secondary biliary cirrhosis of the right hemiliver. This was the ultimate reason for the compensatory hypertrophy of the left hemiliver. Eden’s recurrent cholangitis was possibly due to the stenosis of the main anastomosis – or intrahepatic stones, as previously proposed. This interpretation fits with Eden’s whole story.

#### *Operation n.5: Dilatation of Right Bile Duct Stricture*

On March 5, 1970, Eden underwent his fifth (and last) biliary operation, once again for recurrent cholangitis possibly due to a stricture of the right hepatic duct. Consistently with Cho Grade C results, secondary patency of the anastomosis was obtained after dilatation of the first stricture, but the stricture of the right bile duct recurred and was dilated again. Subsequently, Eden was totally asymptomatic from 1970 to 1975. In 1975 he had a single episode of fever with rigour, but cholangiogram was normal. We wonder if this was a totally separated issue, possibly a urinary infection due to urinary retention from his prostatic cancer. In 1976 he had other episodes of fever up to 38°, but the increased Alkaline Phosphatase, only abnormal test, can be consistent with Eden advanced illness.

Eden’s terminal diagnosis is far from being clear.

#### *Cause of Death*

Anthony Eden was diagnosed with prostatic cancer in 1975, after an episode of fever. Some form of non-surgical treatment was started but there is no evidence of what treatment exactly he had. He survived <2 years after the diagnosis of prostatic cancer. In 1976, after a hospital admission for fever, he was discovered to have enlarged mediastinal nodes and multiple bone metastases. It is likely

that this diagnosis was done with a CT scan. In fact, although the first scanners installed in 1974 were dedicated to the head, body scanning became available in 1976. Although Braasch reports that Eden died of metastatic prostatic cancer, someone mentioned he had liver cancer also and possibly died of it [7]. Adding this possibility to the wide range of hypotheses is appealing.

We understand Eden had a narrow bilioenteric anastomosis which gave him recurrent episodes of cholangitis and it was associated with a stricture of the right hepatic duct, or the right anterior segmental branch. This might have caused a secondary biliary cirrhosis due to chronic biliary obstruction with consequent hepatocellular carcinoma on cirrhotic liver. The fact that he had another operation done in 1962, mentioned by Braasch, went unnoticed by the majority of authors. Braasch states that Eden flew to Boston to have a benign chest wall tumour removed. What was the need to go to Boston to have a simple lump removed? Could not this be done in the UK? We appreciate that, after what happened with his first operation, Eden might not want to risk anything and, mistrusting the British healthcare system, decided to go safe to the US; however, this is not consistent with Eden’s fervent British nationalism. If it was an easy operation, we are sure Eden would have chosen to stay in the UK but in actual facts he decided to go to Boston. Why? This can be consistent with the hypothesis of a subcutaneous or rib metastasis from prostatic cancer or HCC. On the other side, a diagnosis of metastatic cancer is not compatible with the fact that Eden survived 15 years after the excision of the chest lump. Therefore, probably the first hypothesis – Eden mistrusted the British doctors – is the closest to the truth.

#### *Political Effects of Eden’s Complication*

Eden’s cholecystectomy and its sequelae could not come in a worse political period. The world was living a period of wellbeing and growing positivity after WWII, but the Cold War was developing with political and ideological clash between the two superpowers US and USSR. The world was already divided into the two main blocks and isolated conflicts blew up (Korea, Vietnam, Cuban Revolution...), with a permanent risk of a Third World War. One of the main localized conflicts was the Suez Crisis. The almost legitimate nationalization of the Canal by the Egyptian President Nasser prompted a military reaction by Britain, France and Israel, not preceded by any political negotiation or peaceful attempt to re-establish the international agreement. France had been secretly li-

aising with Israel to support its role in the Middle East when Britain was involved into planning a military action against Egypt and his President. Anthony Eden, recently appointed as British Prime Minister, reacted to the nationalization in a way that was by many considered not consistent with his own character and political acumen. He signed a secret agreement with Israel and France to use their Army to regain the Canal and overthrow and kill Nasser without informing the House of Commons. Admittedly, the Cabinet was pretty much involved in his decisions, but he lied to the Commons by not informing them of the ongoing negotiations with France and Israel. His swinging mood created a mayhem at n.10 Downing Street and in the whole Cabinet. On foreign politics, he omitted to involve Britain's strongest supporters, the US and their President Eisenhower, taking for granted that either the US would not be interested, or Eisenhower would support his decisions anyway. This was a huge miscalculation by Eden, and the US withdrew their support to Britain and the British Pound, which devaluated. Meantime, British, French and Israeli aggression to Egypt stimulated the Russian reaction and Khrushchev threatened to start a Third World War.

Being left alone in the Cabinet, Eden was forced to resign, one of the shortest-serving Prime Ministers in Britain's history. The official reason for his resignation was his ongoing illness, with recurrent episodes of cholangitis and constant pain, leading to chronic treatment with painkillers (pethidine and barbiturate), whose depressing effect had to be counteracted by high dose of amphetamines. Eden had been on pethidine, barbiturates and amphetamine for many years, at least since his failed cholecystectomy, officially for clinical reasons. However, we must emphasize that use and abuse of psychoactive drugs was quite common within the political and VIP environment in the '50s and '60s and Eden was not immune to their attraction, to help him – and many of his colleagues including Winston Churchill – reducing the level of stress and tolerating the growing political pressure of his role in that delicate international contingency.

Pethidine, amphetamines and barbiturates impaired his usually acute political analysis and lead to excessive aggressivity and lack of wide vision, distorted his perception of reality, leading to underestimation of the political risks of his decisions, and reduced his decision-making capacity, making him totally isolated within his own political conservative environment. Consequence of this lack of self-awareness and hindsight was a potentially avoidable conflict which left >3,000 casualties, mostly among the Egyptian Army.

The role of Eden's illness consequent to his complicated cholecystectomy and biliary reconstruction on his political attitude during the Suez Crisis was confirmed and emphasized by many Authors [4, 7, 30, 31], but there are many voices singing from a different hymn sheet, stating that his actions were guided by his own character more than the effect of drugs [32]. Eden himself, in an interview in 1967, confirmed his own decisions taken >10 years before:

I am still unrepentant about Suez. People never look at what would have happened if we had done nothing. There is a parallel with the '30s. If you allow people to break agreements with impunity, the appetite grows to feed on such things. I do not see what other we ought to have done. One cannot dodge. It is hard to act rather than dodge [32].

In conclusion, Anthony Eden's clinical history was a succession of technical mistakes and poor medical care that, allowing for the quite primitive diagnostic and therapeutic capabilities in the '50s and '60s, impacted on his own personal history and had long term consequences, possibly leading to his death. The strategic approach used by those who cared for him, including Mr. Hume, Mr. Blackburn, Dr. Cattell and Dr. Braasch, was not totally different by the one we would use today, but we are sure that with the current knowledge, techniques and technology Eden's clinical course would have been different. It is likely that Eden's disgraceful political attitude during the Suez Crisis was at least partially affected by his illness and the strong psychoactive drugs he was on.

Eden's case reminds us that a "bread and butter" operation, as cholecystectomy is considered nowadays, can have disastrous consequences on the patient and his family, on the surgeon and, potentially, on the whole community. We therefore emphasize – and urge the junior surgeons and trainees to do the same – the need to face this operation with the uttermost humility and clinical attention. A biliary leak is one of the possible consequences and complications of gallbladder surgery. His repair should not be left with the operating surgeon, who may not have the specific expertise and appropriate arrangement to perform a biliary repair in a multidisciplinary environment and whose clinical judgement could be biased and confounded by his/her own misperception.

### **Conflict of Interest Statement**

The authors have no conflict of interest to declare.

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## Author Contributions

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