Allen Oldfather Whipple

1881–1963

Jean M. Butte and Elijah Dixon

Dr. Allen Oldfather Whipple. (Courtesy of Samir Johna, MD)

Introduction

Allen Oldfather Whipple, called Oldfather by his closer friends, was born on September 2, 1881, in Oroomisha, Persia (currently Iran), where his parents were working as missionaries. He was always considered the eldest child because his three older siblings died at the ages of 1, 2, and 3 in Persia. The family moved back to the USA in 1896 with the aim of obtaining a better education for their children [1].

Whipple graduated from Princeton in 1904, and then attended Columbia University's College of Physicians and Surgeons, becoming a physician in 1908. He then completed a 2-year internship at Roosevelt Hospital in New York [1].

Whipple was appointed chairman of the Department of Surgery at Columbia-Presbyterian with the rank of professor of surgery in 1921, when he was only 39 years old [2]. Over the course of his career, he introduced the concepts of multidisciplinary teams, prospective collection of data for analysis, and critical assessment of postoperative morbidity and mortality. In addition, he made important contributions to the field including a better understanding of neuroendocrine tumors of the pancreas, the development of the *Whipple procedure*, and insights into portal hypertension [3–6]. He became president of a number of important surgical organizations including the American Board of Surgery and the American Surgical Association. After his retirement in 1946, he completed his career at Princeton where he was a professor of biology and a counselor of students. He died on April 16, 1963, in Princeton, New Jersey. Dr. Allen O. Whipple should be recognized for his tremendous influence in multiple aspects of surgery and for his impact on generations of surgeons.

Living in Persia and His First Years in the USA

Allen Whipple's parents, William and Mary Louise, graduated from seminary school in Ohio and went to Persia to work as missionaries. They went on a *Christian mission* and had nine children, four of whom died in Iran. Whipple was born when his parents had been overseas for 9 years, and his family always considered him the eldest child [1].

The Whipples' stayed in Persia for 25 years in total (1872–1896), with intermittent visits to the USA (1877–1880 and 1889–1890). The young Whipple had several run-ins with medicine including a bout of typhoid fever lasting 2 months and surviving a cholera epidemic in Tabriz that sparked his interest in medicine. However, he first became interested in surgery when his sister had surgery to relieve a small bowel obstruction [1, 2].

Whipple moved back to Oroomiah without his family to attend school in 1894. He lived with the Coans' family and attended the *College Hospital Compound*. In 1895, the wife of one of the local physicians died from pneumonia and the Coans (including Whipple) moved into his house to help him. Whipple was greatly impressed with the doctor, not only for his work but also for the compassion and interest he

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had in his patients. Whipple helped him in his clinical practice and clearly, these activities helped influence his decision to study medicine [1].

The Whipple family returned to the USA to prepare their children for college in 1896. Before leaving Tabriz, they donated all their belongings including their house to create the "Whipple Hospital for Women." Thus, they traveled with minimal goods, without a lot of money, and were supported by their families and friends after arriving. They settled in Duluth, Minnesota, where they rented half of the house where William's brother lived [1]. Allen initially attended the *Duluth Central High School,* where he was seen as a different person because he spoke four languages. The head of his school knew the dean of Princeton and helped Allen to obtain a scholarship to study there.

The Princeton Years (1900–1904)

While at Princeton, Whipple received a full scholarship with a US$ 150 annual stipend. He supplemented the scholarship by tutoring Latin and working at the *Princetonian,* the college newspaper. Years later, he said that this work gave him the ability to express his ideas adequately [1, 2]. He performed well and was in the upper 20–30% of his class. Throughout his time at Princeton, he continued to work hard and eventually went on to manage the Robador dinning club, participated in the Colonial Club, and worked at the Blakeley Laundry. He spent the summer in Evanston teaching a classmate and attended the surgical clinic of Dr. Graham, in the afternoons.

He met many important people in his life while at Princeton. In particular, Charles McClure, a professor of biology, became one of his lifelong mentors. Whipple had planned to attend Johns Hopkins Medical School, but Professor McClure arranged for him to attend Columbia University's College of Physicians and Surgeons with a full scholarship.

Columbia University, College of Physicians and Surgeons (1904–1908)

Whipple continued to excel at Columbia. Of the 160 students in his class, only 79 graduated and Whipple was the third in his class [1]. After graduating medical school, Whipple wanted to continue his training at Roosevelt Hospital, which was the primary teaching hospital of Columbia. He started his residency training on January 1, 1909. However, important changes in the organization of the hospitals occurred during his residency. Abraham Fleuxner conducted studies into the organization of the medical schools of the USA, Canada, and Newfoundland. One of the primary findings was that medical schools should incorporate a teaching hospital when feasible. Roosevelt Hospital was given the option to become the teaching hospital of Columbia University. However, they declined and Columbia subsequently partnered with the Presbyterian Hospital. This decision had an important effect on Whipple, since his surgical mentor, Professor Blake, was transferred to the Presbyterian Hospital. Blake was a senior surgeon, with important experience in and out of the operating room. Despite this setback, Whipple completed 2 years of internship at Roosevelt Hospital even though the standard training included only 1 year of internship. During the first year, he administered anesthetics during the morning, worked in the laboratory, and evaluated patients during the afternoon. He worked as the medical house officer over the next 6 months. During this time, there was a severe epidemic of typhoid fever in New York, and Whipple performed a cholecystectomy on 32 typhoid carriers, interrupting the life cycle of the typhoid *Bacillus* that harbors in the gallbladder and helping to stop the epidemic [7]. During his second year, he functioned as a surgical intern. However, he never completed a formal training program in general surgery.

Whipple was reunited with his mentor when Professor Blake offered him an academic appointment at his outpatient department as the second assistant attending surgeon. Whipple started on January 1, 1911, and was in charge of the fourth-year clerks. During this time, he worked with Dr. Bill Clarke, who was a surgical pathologist, and participated in research into angiogenesis. He also maintained an outpatient practice in the hospital clinic, worked as a part-time surgical pathologist at Englewood Hospital in New Jersey, and maintained his practice in anesthesia and some practice in obstetrics. However, during this time, he was not performing major surgery.

Notwithstanding, the dean considered him an important part of the academic team and appointed him as a junior attending at the Presbyterian Hospital in 1914. This marked his return to the operating room. He was primarily interested in the surgery of the biliary tract as well as postoperative care, specifically in pneumonia, and published at least one manuscript every year.

His Family

In the spring of 1911, Whipple was invited by a friend to meet two young ladies. Miss Mary Neales was coming to New York to be with her sister. After this initial meeting, the two maintained the relationship, and Dr. Whipple visited her in Boston, when she underwent an appendectomy. They were married on September 26, 1912, at Woods Hall,

Massachusetts. They were married for 47 years until her death in February 1959 from a possible myocardial infarction.

They had three children—Mary Allen Whipple (1913–1990) who married Dr. Richard Being, a famous cardiologist; Allen Oldfather Whipple Jr., (1915–1963) who studied history at Princeton; and William Neales Whipple (1917–1933), who was involved in a severe accident near New York. Dr. Whipple was called in to evaluate his son and traveled with him in the ambulance back to Presbyterian Hospital. Unfortunately, he succumbed to his wounds and passed away after emergency surgery.

Contributions to Surgery

Dr. Whipple contributed to the surgical field in many different ways [8–10]. However, he was specifically interested in the spleen (especially the after effects of removal) and portal hypertension, determining that the latter was a consequence of a liver disease. In 1945, he published their experience of 1189 patients treated in 17 years in *Annals of Surgery* [4].

Much of his research focused on postoperative complications. Indeed, he noticed that many patients developed a particular form of pneumonia after surgery. He studied this finding and wrote a paper called "A study of postoperative pneumonitis." In this series, 97 of 3719 (2.3%) patients developed this condition [8]. This was the first study to define postoperative atelectasis and its clinical implications.

Whipple created the first system to record the inpatient and outpatient records into a single document in 1916 and emphasized this comprehensive collection of data in his first paper about pancreatic disease published in 1918. That year he presented a protocol for the collection of information on patients with diseases of the biliary tract and pancreas, which was one of the first prospective protocols.

Dr. Whipple became interested in pancreatic tumors, especially in *islet cell tumors of the pancreas*, while he was studying the spleen and portal hypertension. He initially studied the insulinoma, which was the first hormone-secreting tumor of the islets of Langerhans to be recognized. The concept of "spontaneous hyperinsulinism" was first reported in 1924 within a year of the discovery of insulin by **Banting** and **Best**. Patients presented with symptoms similar to those of an insulin overdose. After **William Mayo** first described hyperinsulinemia from a malignant islet cell tumor in 1927, and Rosco Graham in 1929 successfully removed the first benign insulinoma, many patients were operated on for symptoms of hypoglycemia, yet the success of finding an insulinoma was only 32%. It was Whipple who put together a series of 62 patients from the world literature operated on for hypoglycemia and developed a clinical tool to help establish the diagnosis of an insulinoma from other causes of hypoglycemia [5]. In this landmarked article, Whipple introduced his Whipple's triad, which consisted of (1) clinical symptoms of hypoglycemia following fasting, (2) low blood glucose levels at the moment of symptoms, and (3) temporary relief of symptoms with the administration of glucose [3, 5, 11]. By the time he retired, Whipple had operated on 39 cases of insulinoma, the largest published series at that time (Table 1). Whipple's triad is still utilized today in the diagnosis of insulinoma.

Table 1 A summary of Dr. Whipple's experience treating neuroendocrine tumors of the pancreas

Characteristics	*N*
Patients explored	39
Tumor found (patients)	34 (87%)
Operations	*N*=44
Simple excision	21
Partial pancreatectomy	10
Reoperation and resection	7
Whipple procedure	1
Exploration and failure to find the tumor	5
Diagnosis	*N*=43
Adenoma	27
Carcinoma (functional)	3
Carcinoma (nonfunctional)	1
Probably malignant	9
Adenomatosis	3

The Whipple Procedure

Until Whipple's innovations in pancreatic surgery, the formal resection of the pancreas was a highly morbid procedure. Between 1882 and 1905, 21 surgeons removed part of the head/body/uncinate process of the pancreas in 24 patients, with a mortality rate of 53% in 19 [1]. Codivilla performed the first pancreatoduodenectomy in 1898, but the patient died 24 days after surgery. That same year, Dr. Halsted performed the first local resection of a carcinoma of the ampulla de Vater [1].

Whipple observed that the main problem associated with the resection of the head of the pancreas was bleeding due to the hypocoaguable state caused by jaundice. It was not yet known that the underlying issue was a lack of vitamin K (a fat-soluble vitamin) absorption due to the disruption of the biliary system [12, 13]. However, the discovery of insulin in 1921, the description of human blood groups in 1930, and the discovery of vitamin K in 1929 helped improve the outcome of pancreatic surgery significantly. Whipple performed the first two-stage Whipple procedure in 1934 [6]

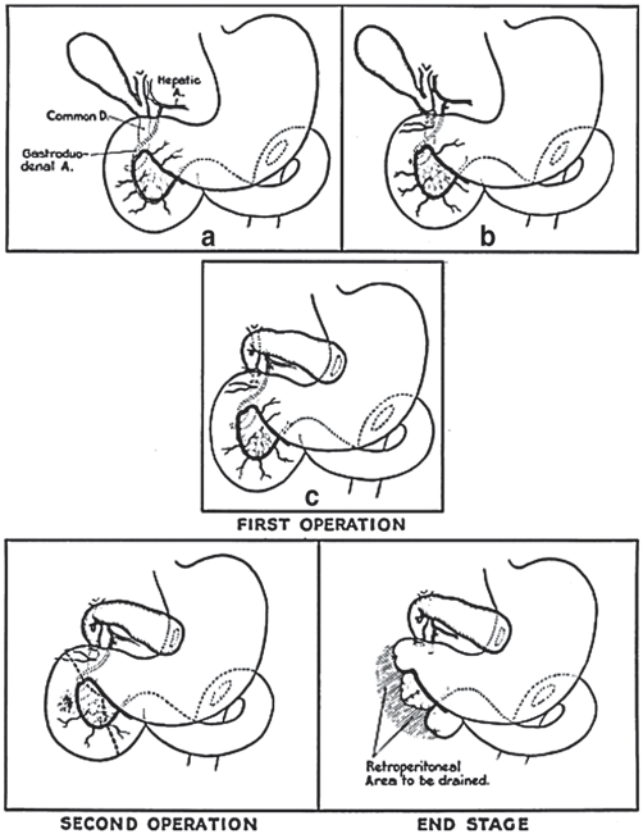

Fig. 1 The two-stage Whipple operation. (From Whipple et al. [6]. Reprinted with permission from Wolters Kluwer Health)

(Fig. 1), while the first one-stage procedure was not performed until 1940 [3]. On March 6, 1940, Whipple operated on a 33-year-old woman who was thought to have a possible gastric cancer. During the operation, he felt a mass in the pylorus and transected the stomach in the middle part. He examined the posterior wall and did not find a tumor in the pylorus, but instead found a small tumor located in the head of the pancreas. He performed a one-stage pancreaticoduodenectomy, removing the distal part of the stomach, the head of the pancreas, the duodenum, and the distal bile duct. He then closed the pancreatic stump and duct and anastomosed the bile duct to the stomach (Fig. 2). The patient had made an excellent recovery. The final pathology was a glucagonoma, which was the first reported glucagonoma resected. The patient died 9 years later from liver metastases. Whipple presented the case at the New York Academy of Medicine after 5 years of follow up and published the operation in *Annals of Surgery* that year [3]. Whipple would later publish a series comparing the mortality rate of 38% in eight patients treated with two-stage surgery and 31% in 19 patients treated with one-stage surgery lending support to the superiority of a one-stage procedure.

Involvement in Surgical Societies

Whipple was active in many surgical societies at the time. He served as president of the American Board of Surgery (ABS), the American Surgical Association (ASA), and the Society of Clinical Surgeons (SCS) among others. One of his great passions was surgical training. In 1935, he presented a paper "Opportunities for graduate teaching of surgery in larger qualified hospitals" [14]. The president of the ASA subsequently recommended creating an American Board of Surgery to help distinguish surgeons practicing surgery at a higher level and Whipple was vice-chairman of the initial task force. Whipple served as vice-president of the ABS for 4 years and president for another 2 years. Whipple served as the chairman of the commission that selected the questions for the first certifying examination. Whipple was also a governor of the ACS between 1938 and 1948 and received the gold medal from the American Medical Association for his distinguished service in 1951 [15, 16]. He served as president of the American Surgical Association in 1939 and his presidential address expounded on the subject of wound healing. Whipple was elected president of the Society of Clinical Surgeons in 1935 and traveled to Europe with the Society in 1937. The night before his departure, his mother developed a bowel obstruction from an inoperable tumor. He traveled to Wisconsin to see her, and she died 2 days later. He then joined his colleagues in Europe.

Time at Memorial Hospital (1947–1951)

In January 1961, Whipple received the Judd award from Memorial Hospital in recognition of his contribution to the field of cancer. He was subsequently approached by the director of the Memorial Hospital to serve as the clinical director. Although Whipple had planned to go to Beirut after retiring from Presbyterian Hospital, he ended up taking the position. His main objectives were to develop an academic residency, increase the standards, and create an autonomous surgical service. He created the most modern and well-equipped experimental laboratory of the country 1 year before retirement. Whipple did not like administration, finding the job very uninteresting, and happily left for retirement [1].

Retirement

Whipple moved to Princeton where he was appointed as an advisor to the students and continued with his studies on the splenic circulation in the laboratory of Professor Parpart, publishing these results in 1954 [17]. Whipple was honored

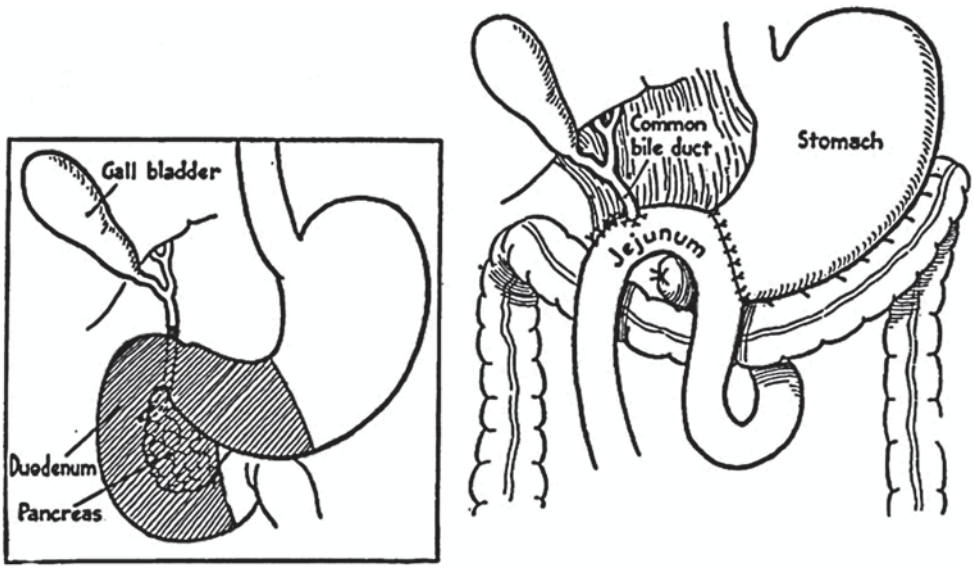

Fig. 2 The one-stage Whipple operation. (From Whipple [3]. Reprinted with permission from Wolters Kluwer Health)

with a dinner in the Grand Ballroom of the Plaza Hotel in New York City on September 22, 1952. The *Whipple Surgical Society* was created that day and consisted of 217 surgeons who had been trained by Whipple. The Whipple Society closed in 1978 but reopened in 2003 [18].

Whipple continued on at Princeton as a visiting lecturer and professor of biology. He also became a trustee of Princeton University from 1943–1952 and was granted a doctor of science in September 1956 followed by the Woodrow Wilson Award in February 1958 for his lifetime of achievements. During this time, he was also the chairman of the advisory committee that guided in the building of a hospital in Shiraz, Iran.

Dr. Whipple attended the annual meeting of the ASA in 1961, but had two episodes of chest pain and returned immediately to Princeton. He was transferred to Presbyterian Hospital and was admitted for 6 weeks. He was found dead possibly of a myocardial infarction in his house, in Princeton, on April 16, 1963. His son had died just 8 days before. Allen O. Whipple will always be recognized as a pioneer in surgery and his work in the treatment of pancreatic disease. Surely, many generations of health care professionals will continue to refer to Whipple's triad and the Whipple procedure.

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1. The life and times of Allen Oldfather Whipple. *The Missionary and the Surgeon*, by John M Howard.
2. *The Memoirs of Allen Oldfather Whipple: The Man Behind the Whipple Operation* by Allen Oldfather Whipple, Samir Johna, M.D. (editor), Moshe Schein, M.D. (editor)

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