APPENDIX

FROM THE NEUROLOGY INDIA TREASURE TROVE: The Last Days of Harvey Cushing

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Just 30 years have elapsed since the death of Harvey Cushing of coronary occlusion and myocardial infarction at the New Haven Hospital on October 7, 1939. At his expressed wish, a post mortem examination was performed that same day whose findings have not previously been published in full. The detailed report of this examination is now provided to NEUROLOGY INDIA at the suggestion of Dr. S K Pandya of Bombay and at the request of Dr. Anil Desai, editor of this journal.

Almost as soon as the examination was completed, inquiries began to arrive from former students and colleagues of Cushing regarding certain aspects of his earlier illnesses with which they were familiar. Merrill Sosman was intrigued to learn that the peptic ulcer whose course he followed roentgenographically had completely healed. Arnold Klebs* of Switzerland, Cushing’s close friend of many years, in a letter which is reproduced here, (Plate XL) expressed special interest in the evidence of the residual tuberculous lesions that were found in the pulmonary apices. Others wished to know the true nature of the illness which Cushing himself had diagnosed as ‘encephalo-radiculitis’ in 1918 in France, and were astonished to learn that this was caused by a sudden thrombotic occlusion of the abdominal aorta. In a ruminating mood a year or two before his fatal illness, Cushing expressed an interest to me regarding the cause of the parasthesia and weakness of the fingers of his left hand. He surmised that these symptoms were produced by focal cortical softening. How very accurate his diagnosis was!

Plate XL (A clear copy of this letter was obtained through the courtesy of Dr. Reeta Mani, Department of Virology, NIMHANS.)
A number of misconceptions have arisen regarding some of the findings established by the post mortem examination. One of the more common of these is that a large colloid cyst of the third ventricle was present. This is inaccurate both as to size and nature of the lesion. In reality, the cyst was but 6 or 7 mm in diameter and was functionally of no moment since it did not block the foramen of Monro. Also, it represented a simple cyst of the choroid plexus rather than a ‘true’ colloid cyst - it had no ependyma-like lining cells in its wall.

**Reminiscences**

The last years of Cushing’s life, from his arrival as Sterling Professor at Yale in 1933 to his terminal illness, was marked by repeated episodes of vascular disease affecting his lower extremities that frequently required his taking to a wheel-chair. This was diagnosed as a form of Buerger’s disease and he was advised on several occasions to permit amputation of the involved toes. But he would hear none of this! Especially he was warned not to smoke since this was regarded as being particularly deleterious. Knowing full well, therefore, of the disapproval of his surgeon and above all his secretary, Miss Stanton, he kept a corn-cob pipe secretly in his desk and took occasional puffs when not observed by the censors. At the approach of his secretary, he would hastily return the pipe, in a small-boy fashion, to a desk drawer from which there sometimes continued to rise a feeble smoke-ring. Since little vascular disease was actually found below the femoral arteries, he evidently suffered small injury, as far as the vessels in his legs were concerned, from this habit.

His last years at Yale were by no means unhappy. There was an almost constant flow of visitors to his office at the medical school and to his home on Whitney avenue in New Haven. One such visitor, Dr. Bernard Sachs of Tay-Sachs fame, on seeing Dr. Cushing wheeled into my laboratory by his chauffeur, said in an aside, ‘What’s happened to this young generation?’ Cushing was 68 years old at the time and Sachs, who was still quite spry, was some 10 years older.

In 1936, during the national presidential campaign, Franklin Delano Roosevelt whose son was married to a Cushing daughter, paid a visit at the Cushing home amidst considerable publicity. For days after this visit, Cushing sported a huge sunflower button on the lapel of his coat to the delight and amusement of students and staff. This was the campaign symbol of Alfred Landon of Kansas, the Republican candidate for the presidency.

His scientific interest and productivity did not abate. He conducted weekly conferences on brain tumors for students and staff at the New Haven Hospital. He wrote and published the remarkable book on Meningiomas with Louise Eisenhardt during those years at Yale. He continued his absorbing interest in collecting Vesalius editions, and time after time I received telephone calls from him to spend an evening at his home to view a new acquisition. On such occasions I met William MacCallum, Professor of Pathology at Johns Hopkins and one of Cushing’s close friends, as well as Ernest Sachs, Professor of Neurosurgery at Washington University in St. Louis.

For many years, Cushing had been interested in the role of the basophil cells of the pituitary gland in the production of the syndrome which later was to bear his name. At his instigation I undertook a study of these cells in the pars nervosa, and after studying 200 glands in serial sections concluded that there was no evidence that they were causally associated with either hypertension or other features of the syndrome. This undoubtedly was a disappointment to Dr. Cushing as it was to me, but he took it in a cheerful spirit. As a token of our abortive collaborative effort he presented me with his inscribed photograph which is here reproduced. (Plate XXXIX)

Cushing delighted in playing pranks and in telling stories. At this he was a master and was at his best during the frequent luncheons he gave at his home for visitors and friends at the hospital. The butts of his stories were frequently at his table and were his close friends. On one such occasion he told the following about John Fulton:
At the end of an International Congress of Neurology held in Rome, there appeared the Romanian ambassador with an invitation from King Carol (he of Madame Lupescu fame) to any of the visiting scientists to visit Bucharest for special honors. Fulton, among several others, accepted the invitation and travelled to the Romanian capital. On the appointed day and after many hours of weary waiting, the King arrived and addressed his honored guests briefly and in Romanian. He kissed Fulton on one cheek, then on the other, and hung a purple ribbon with a large bronze medallion around his neck. Thereupon he was dismissed. The inscription was in Romanian, of which Fulton knew not a word. Before leaving the palace grounds he spotted a gardener who, upon inquiry, admitted to a knowledge of English. When shown the medallion, the gardener, with great alacrity jumped to attention, clicked his heels in the best military manner, and spoke: 'Sir, you have just been created a Knight of the Order of Chastity! Third Class.'

**Autopsy Protocol**

A 4706

Dr. Harvey Cushing - W M

Age 70 yrs. - Hosp. No. A 32392

Died: Oct. 7, 1939; 2:45 A.M.

Service: Medical

Autopsied: Oct. 7, 1939; 10:00 A.M.

H M Zimmerman, M.D.

**Clinical History**

**Chief Complaint:** The pt. was admitted to the N.H.H. on Oct. 4th, 1939, at 4 o’clock in the afternoon because of a gnawing and persistent pain under the lower third of the sternum.

**Present Illness:** The pt. had felt quite well for the past 2 years, but 10 days ago he began having occasional vague and transient epigastric or substernal discomfort and a little heart-burn.” At 10 in the evening on the 3rd October the pain took on a gnawing character, was not severe, but persisted throughout the night with varying intensity. At noon on the 4th, the pt. vomited, and vomiting recurred on the way to the hospital. The pain did not radiate and there was no ‘squeezing’ sensation. Pantopon® brought relief, but not codein.

**Present Examination:** On admission to the hospital, the pt. was somewhat drowsy and confused. There was no dyspnea and no cyanosis. The jugular veins were not engorged. Heart sounds were practically inaudible. Blood pressure was 90 systolic and 45 diastolic (usual pressure was 160 to 180 over about 100). The heart sounds were irregular. The abdomen was very slightly tender without there being any epigastric spasm. The temperature was 98° F., and the respiratory rate 20 per minute.

**Past History:** In 1918, while Dr. Cushing was overseas on war duty, he had an unusual illness which he believed was a form of encephalo-radiculitis and was characterized by diplopia, bilateral facial weakness, numbness in all extremities and absence of all reflexes. He was in hospital for 2 months. After which he returned to this country and gradually returned to work. It was his belief that he was never quite so well after as before this illness.

Since 1923 he has noticed increased claudication of the legs brought on by exercise. Dr. William Thayer of Baltimore could not feel the patient’s popliteal pulsations on either side as much as 16 years ago. In 1931, the left big toe became blue and sore, requiring rest in bed a part of each day for 6 weeks. This treatment resulted in a complete cure.

About Sept. 1st, 1933 the patient had an attack of diarrhea associated with vague, gnawing epigastric pains and loss of appetite. A diagnosis of ulcer on the lesser curvature of the stomach was made from a roentgenogram by Dr. Merrily Sosman of Boston, and the patient was treated with a bland diet and magnesium and calcium powders. This therapy relieved epigastric discomfort, and after 2 weeks another roentgenogram showed improvement in the appearance of the crater. The following month Dr. Cushing went abroad, which marked a period when it was impossible to follow any dietary regime. As a result, he was in discomfort much of the time. On the return crossing the weather was rough, adding to the discomfort, and he vomited on one occasion. The right big toe began to be painful and the skin became ulcerated. It was this combination of circumstances that necessitated his entrance into the New Haven Hospital in Nov. 1933.

The blood pressure at that time was 140 over 75. In addition to a rather decided tenderness elicited by light palpation of the epigastrium and left upper quadrant of the abdomen, it was found that both feet were cold and there were no pulsations in the dorsalis pedis, posterior tibial and popliteal vessels on either side. Gastric analysis disclosed an increase in the free HCl acid, both in the fasting specimen and after alcohol and histamine. Roentgenography revealed an ulcer on the lesser curvature of the stomach. The stools were guaiac positive. Sippy 1 diet with A and B powders after each meal resulted in striking subjective improvement and a practically normal stomach by roentgenography (Feb. 8, 1934).

The lesion of the right big toe was attributed to arteriosclerosis and was treated with dressings, Buerger’s exercises and rest. When discharged from the hospital on March 9, 1934, the toe had sufficiently healed to permit the patient to be up and around on crutches.
**Family History:** The patient’s father had claudication of the extremities and died at 86 years of age of cardio-vascular disease. A brother died at 66 of coronary occlusion. The remainder of the family history is irrelevant as regards the patient’s present illness.

**Course in Hospital:** At 11 o’clock in the evening on the day of his admission to the hospital (Oct. 4, 1939) the patient became restless, cyanotic and complained that his right leg felt numb, aching and weak. Voluntary motion, however, was present in both legs but the deep tendon reflexes were absent. Pantopon® brought marked relief in 15 minutes, the blood pressure having risen to 150 systolic and 80 diastolic. The heart sounds were regular, the rate about 75 per minute, and of improved quality. An electrocardiogram disclosed partial heart block during this episode, and the following morning the pulse again was 54 per minute, indicating apparently a 2 to 1 block.

Cheyne-Stokes respiration required the use of an oxygen tent. Twenty-four hours after admission the patient was in great distress, his colour was grayish rather than cyanotic and rales appeared at the bases of both lungs. On the 6th of October, an electrocardiogram revealed complete A-V block, with the ventricles beating at a rate of 60 per minute. Intraventricular block also made its appearance. At about 2 A.M. on Oct. 7, the heart rate, which was 30 per minute, became irregular and stopped altogether 45 minutes later.

**Lab Findings:** RBC 4.1 million; Hgbn. 88 per cent. (13.5 gms); WBC 11,000, Non-segmented cells 10 per cent.; segmented cells 76 per cent.; lymphocytes 8 per cent.; large mononuclears 6 per cent.

**Clinical Diagnosis:** Coronary occlusion with complete heart block.

**Gross Notes**

**Body:** The body measures 172 cms. (5 ft. 8 inches) in length and weighs 63.6 kilos (140 pounds). Livor mortis* is quite extensive over the back and shoulders and rigor is present to a moderate degree in the extremities.

The scalp hair, which is slightly thinned over the vertex, is nearly completely white. A dilated and tortuous vessel is seen beneath the skin of each temple. There is no nasal discharge or septal deviation. The conjunctivae are pale, contain no petechiae and are completely translucent over the corneae. Each pupil measures 6 mm. in diameter; they are both perfectly round and regular. The tongue is coated with a dried brown crust of a millimeter thickness. Several teeth in the upper denture are replaced by a plate and most of the other teeth are under extensive repair. This is also true of the lower set of teeth. The posterior pharynx is not red and is not covered by exudate. The tonsils are small; their crypts are apparently empty.

A small, mulberry-like papilloma is present over the left scapular ridge. The skin over the back, sacrum and trochanters is intact. The body is quite well nourished-to a much better degree than seemed possible to one who knew the patient for several years past. The panniculus adiposus averages about 2 cm. in thickness. There is a slight fullness of the abdomen, which bulges a little above the level of the anterior chest wall, but the abdominal muscles are soft and not in rigor. A well healed scar measuring 14 cm. in length is present in the lower right rectus region. The muscle bundle below the scar seems ‘bunched’ and doughy in consistency. There are no visible external hemorrhoids, no rectal or urethral discharges. The external genitalia and the hair distribution are of the normal adult type.

It is apparent that the lower extremities are less well developed than the upper and they seem even somewhat atrophic, but in a symmetrical manner. They are definitely but almost imperceptibly shortened, which is determined only from the fact that they contrast with the otherwise well developed and proportioned trunk and upper extremities. The muscles of the thighs and calves are a little flat. The phalanges of the left middle toe are absent, and a healed operative scar indicates their surgical removal. The nails of all the toes are atrophied and are fused with the skin over the distal phalanges. There are no ulcerations on the toes, but the tips of the right 2nd is purple in color. The skin over the right tibia is abraded, the abrasions being covered by scales which are painted with tincture of iodine. Two or 3 needle puncture wounds from clyses are seen in the skin over the anterior surfaces of the thighs. The skin over the upper extremities is intact.

Following the usual Y-shaped incision, first the abdominal and then the thoracic cavities are exposed to view. The former is lined by a smooth and glistening serous surface, which also covers the intestines and other abdominal viscera. There is no exudate present, and only a few cubic centimeters of clear lemon-yellow fluid. A narrow but tough fibrous adhesion is seen between the cecum and the anterior abdominal scar, the residuum of an appendectomy. The greater omentum covers the intestines in an apron-like fashion without being adherent to any viscus. When reflected upwards, there is exposed to view a delicate fibrous tag which extends from the neck of the gall bladder to the anterior surface of the pylorus of the stomach. At the latter point of attachment there is seen a nodular elevation which measures slightly over 1 cm. in diameter and about 0.5 cm. in height. To palpation, it has the firmness of dense fibrous tissue and will be described in more detail below. The disposition of the remainder of the abdominal organs is normal. It can be determined that the dome of the diaphragm extends upwards to the level of the 6th rib on the right and the 7th rib on the left. The anterior margin of the liver is down 4 cm. below the ribs in the midclavicular line and 9 cm. below the xiphoid process. It is not seen below the ribs on the left. When the loops of small intestine are separated, the major portion of the abdominal aorta is visible as a distended tube and is found to be surprisingly firm to palpation. The firmness is more striking in the lower 4 or 5 cm. and extends for a similar distance into the right common iliac artery and for about 2 cm. into the left common iliac. The condition is strongly suggestive of thrombosis-these vessels will be described fully below.
Immediately upon elevating the anterior chest plate, both pleural cavities are found to be filled with clear straw-coloured fluid which is free from fibrin. The fluid in the left cavity measures slightly more than 400 c.c., and that in the right cavity measures exactly 1000 c.c. In consequence of this, both lungs are considerably compressed and are somewhat flattened against the mediastinum. The pericardial sac is rather distended and is found to contain, in addition to the obviously enlarged heart, somewhat less than 100 c.c. of turbid, yellow fluid. A smear of this fluid stained by the Gram method discloses both fibrin and chains of gram-positive cocci. The pulmonary artery is opened in situ and is found to be filled with dark, postmortem clot; there are no thrombi or emboli. Having aspirated the thoracic fluid, a number of velamentous adhesions are found between the diaphragmatic pleura and the base, the mediastinum and the medial surface of the left lung. A much denser cord of fibrous tissue is seen between the apex of the left pleural cavity and a pleural scar which lies 1 cm. below the apex of the lung. On the right side, a similar adhesion is attached to the antero-lateral surface of the lung about 2 cm. below the apex.

Heart: The heart, which has already been mentioned as being enlarged, weighs 494 gm. The epicardial surfaces are somewhat dull and lusterless from the presence of a thin coat of fibrin which is loosely adherent. There is a pale gray zone of discoloration, about 3 cm. in diameter, which is slightly soft to palpation and is situated in the anterior wall of the left ventricle near the interventricular septum. The coronary arteries are tortuous, and firm to hard on palpation. They are dissected off from the heart, sketched, decalcified and sectioned at intervals of 3 to 4 mm. with the following results: the lumen of the left coronary is greatly reduced in size and the wall is mottled and streaked with vasa. The wall is fibrous rather than atheromatous. Throughout the anterior descending branch, the lumen is patent to about 50 per cent. The mid-portion of the circumflex branch, however, has a very small opening and the wall is composed of concentric rings of fibrous tissue whose outer layers are quite vascular. Just beyond this point, the vessel is completely occluded by what appears to be a canalized thrombus. The lumen of the right coronary artery is open only to about 10 per cent, the narrowing being due to extensive atheromatous change. Just beyond the point where the marginal branch originates, the right coronary is completely filled with a soft, crumbling atheroma and, immediately beyond this, the lumen is filled with what appears like an old organized thrombus. The latter is gray and firm and has streaks of red. The wall contains vasa from which there seems to have been some hemorrhagic extravasation. The terminal 2 or 3 cm. of this vessel are alternately patent and occluded by gray, apparently old and organized, thrombi.

The right auricular appendage is found to bulge and is a livid purple externally. This is due to a thrombus which is red in the center, gray on the margins adjacent to the endocardium, and firmly fixed in situ so that it cannot be removed without crumbling. Apparently, it is undergoing organization. The cavity of this auricle is somewhat increased in size and the wall is slightly thickened. The tricuspid valve ring is quite stretched, measuring 14 cm. in circumference; the valve cusps are not thickened.

The cavity of the right ventricle is rather large due to chronic dilatation—the papillary muscles are flattened. There is some widening of the conus pulmonalis. The pulmonic ring measures 7.5 cm. The cusps are thin and delicate. Where the endocardium lines the lateral walls of this cavity, it is deep red in color and smooth and glistening. Over the interventricular septum, however, it is somewhat opaque and yellowish in color. The septum is split longitudinally from the apex to the auricular junction, disclosing extensive zones of anemic necrosis. This is obvious from the parboiled appearance of the myocardium, its yellow color and soft consistency. The right ventricular wall measures 5 mm. in thickness.

A thrombus fills the left auricular appendage, but this clot is of more recent origin, being more uniformly deep red in color. The endocardium of this cavity is thickened and milky white in color. The auricular wall is definitely thicker than usual and cavity is increased in size. There are no healed lesions on the cusps of the mitral valve, whose ring measures 10 cm.

The papillary muscles of the left ventricle are greatly flattened. Their chordae tendineae are long and gracile, inserting in the usual fashion on the line of closure of the mitral valve. This cavity is the most extremely dilated, the dilatation being most prominent in the apical portion where deep recesses are seen between the muscular trabeculae. The wall at the apex is surprisingly thin. In its mid-portion it measures 6 mm., which is but slightly more than the thickness of the right ventricle. The endocardium of the apical portion is milky-gray like that of the left auricle; elsewhere in the cavity, it is translucent and shining. To its apical portion are attached flattened, buff colored, friable thrombi. Numerous silvery gray strands of scar tissue are seen in beneath the gray patch on the epicardium. The aortic ring measures 8 cm. There are no lesions which affect the aortic cusps. Behind the latter, the sinuses of Valsalva are of average depth. The coronary artery orifices are neither narrow nor otherwise obstructed. Atheromatous plaques of a large size are present beneath the intima of the ascending portion of the aorta. The wall of this vessel is greatly thickened both by the subintimal atheroma and the fibrosis in the media and adventitia.

Lungs: The left lung weighs 472 gm. As already noted, fibrous adhesions are present in the diaphragmatic, mediastinal and subapical surfaces of the visceral pleura. The latter is mottled with numerous stellate and linear streaks of black anthracotic pigment. Three large emphysematous blebs or bullae are present beneath the visceral pleura on the anterior margin of the lower lobe. Fine, retracted scars seem to account for the sub-divisions of the zone of emphysema into these bullae. The subapical pulmonary scar is puckered and extends for nearly 1 cm. into the underlying parenchyma; its surface area measures 2 x 3 cm. There is no caseation or calcification in this scar. The hilar nodes are slightly larger than usual. They are deeply pigmented with dust but are succulent, nevertheless. The pulmonary artery is found unoccluded to its finest divisions. There is no evidence of either bronchitis or bronchiolitis, but a pink frothy fluid fills the entire bronchial tree. The parenchyma is deep red in color, boggy and water-logged. This has obliterated the normal crepitus, but there are likewise no definite zones of consolidation.
To the anterior surface of the right lung, which weighs 606 gm., a fibrous tag is adherent a short distance below the apex. This is the site of a calcified tuberculous mass which lies beneath the pleura and has a caseous center. The mass measures nearly 2 cm. in diameter and is associated with a fibrosed but non-calcified or caseous hilar lymph node. This, as well as the remainder of the nodes, is black with pigment. There are no emphysematous zones in this lung, but otherwise it resembles the left one in all details.

**Spleen:** There are no unusual features in this organ, which measures 11 x 7 x 3 cm. and weighs 163 gm. The capsule is livid in color and wrinkled. On section, the trabeculae appear as unduly prominent gray strands in an atrophic pulp.

**Stomach and duodenum:** It has already been mentioned that a narrow fibrous adhesion, several centimeters in length, binds the neck of the gall bladder to a nodular elevation on the anterior surface of the pylorus. The stomach is not distended, and there is no thickening of the remainder of the pylorus which could give rise to obstruction. Neither the anterior nor posterior surfaces of the stomach are adherent to any of the adjacent, especially retrogastric, structures. When opened, very little gas escapes from the stomach, which contains a small quantity of white, partially digested curd. The gastric wall is not thickened, and this is true also of the pylorus except for the site of the 1 cm. nodule. The latter seems to be in the muscular coat and has the appearance of a leiomyoma. The fundic mucosa is intensely congested and apparently contains many petechial hemorrhages. The mucosa of this portion as well as of the remainder of the stomach is hyperplastic, as in chronic gastritis. On the posterior wall of the pylorus, it is quite flat over two small linear areas, neither one of which is more than ½ cm. in width and 2 cm. in length. These may possibly represent the sites of the old ulcer-they extend for several millimeters into the first portion of the duodenum-but the wall beneath them is neither thickened nor scarred. Nor is there any evidence of scar on the serosal surface.

The duodenal mucosa is just as intact as the gastric. It is free from all traces of ulceration, past or present, except for the flattened areas which are extensions from the pylorus. The ampulla of Vater is seen as a small nodular elevation into which empty both the common bile duct and the pancreatic duct. The former is shown to be patent by the expedient of squeezing the gall bladder, which produces a free flow of bile. The latter is found to be patent on probing.

**Pancreas:** This organ, which weighs 95 gm. minus most of the surrounding adipose tissue, has the usual tawny, lobular appearance. Although a small amount of fatty tissue is found among the lobules of the gland there is no excess connective tissue, even in the head.

**Gall bladder:** There are a little over 50 c.c. of thick, viscid, almost black bile in this organ. The wall is not thickened and there are no calculi. The cystic duct is neither thickened nor dilated, although a fibrous tag binds it to the pylorus. It empties into the common duct in the usual manner. The ductus choledochus is not dilated or obstructed.

**Liver:** The weight of the liver is 1400 gm. and it measures 23 x 19 x 6.5 cm. The capsule of Glisson is thin, smooth and translucent. The hepatic artery, portal vein and hepatic veins are all unobstructed. Minute, dark red zones are uniformly distributed throughout the dark brown liver and probably represent congested central veins and sinusoids.

**Adrenals:** Together the adrenals weigh 20 gm. They have the usual triangular shapes with well defined chrome yellow cortices and dark brown central medullary portions. No cortical hyperplasias or adenomas are seen macroscopically.

**Kidneys:** The right kidney, which is the smaller of the two, weighs 142 gm. and measures 10x6x3.5 cm. Its capsule is not unusually adherent, and when pulled away, leaves an essentially smooth surface of deep red color. There are a few small scars in the cortex, which averages 4 mm. in thickness. The cortical striations are distinct, as are the pyramidal rays. Many of the renal vessels have thickened walls and small lumina. They project above the flat surface of the sectioned kidney due to a striking loss of elasticity. The renal artery, although thickened and sclerotic, is not occluded. The renal calyces, pelvis and ureter are not abnormal.

The left kidney weighs 164 gm. It is even deeper red than the right, but its capsule can be stripped with equal ease. When this is accomplished, large yellow patches come to view on the slightly scarred surface. The striations in the latter are blurred. The yellow patches extend in roughly wedge-shaped fashion towards the renal pelvis. These several infarcts have narrow margins of hemorrhage. The pelvic mucosa is pale, the smaller renal vessels are changed in the same manner as those in the right kidney. The main renal artery is unoccluded, but its walls are thick and extensively altered by atheroma. The ureter is neither dilated nor inflamed.

**Urinary bladder:** About 50 cc. of clear, lemon-yellow urine fills the bladder whose wall is neither thickened nor trabeculated. The mucosa is pale and smooth.

**Prostate:** This is a small, soft gland with an adenomatous nodule in the left lateral lobe. Amber-colored material is seen in the dilated cyst-like acini throughout the gland and more especially in the adenoma. The latter is but 5 mm. in diameter. The seminal vesicles are filled with a brownish fluid. They are not fibrosed.

**Gonads:** These glands are somewhat soft, contain no scars and have tubules which can be strung out readily.
**Intestines:** The entire ileum is lined by an intact mucosa, which is pale for the most part. At periodic intervals, however, it is slightly congested, and in 2 or 3 places, a few petechiae are seen. The large intestine is no more strikingly altered than is the small. Both portions of the intestinal tract have non-edematous walls, which are also not thickened in any other way. The serosa is pale and glistening. In the descending colon, there are found a few small diverticula which are filled with fecal material and disclose no inflammatory reaction. There are no polyps in the rectum and no internal hemorrhoids.

**Blood vessels:** The aorta is detached from the heart about 5 cm. above the aortic valve ring and is removed from the body with the celiac axis, mesenteric and renal arteries, common iliac and internal and external iliac arteries attached. It is fixed in 10 per cent formalin for 24 hours and then carefully decalcified. At the conclusion of this process, transverse sections are made at 5 mm. intervals and the following changes are noted (see Fig. 1 Plate XLI):

![Image of transverse sections of entire aorta](image)

**Fig. 1. Transverse sections of entire aorta from 5 cm. above aortic valve (left upper corner of illustration), through bifurcation of the common iliac arteries, and down through the internal and external iliacs. See detailed description in the Protocol.**

The arch of the aorta is somewhat wider than normal and the wall is considerably thicker. This is due to a thickening of the adventitia, but more especially of the intima, which is extensively altered by atheroma and is ulcerated. The same process is found extending throughout the thoracic portion. From the level of the celiac axis to that of the renal arteries, a fresh blood clot forms a mural thrombus. The latter lies against the orifice of the left renal artery whose walls are enormously thickened by arteriosclerotic changes. The fresh mural thrombus increases in size progressively downwards until it completely blocks the lumen of the aorta at a point just below the origin of the inferior mesenteric artery. From here to the point of bifurcation of the aorta, the latter vessel is distended and is surprisingly firm to palpation. This is produced by an old laminated and apparently partially organized thrombus.

The left common iliac artery has an atrophic appearance, and in diameter is half that of the right iliac. Its lumen is completely filled with a gray, firm organized clot that extends into the external as well as the internal iliac arteries. The right common iliac artery lumen is filled with a much more recent thrombus, but the internal and external iliac vessels on the right have the same appearance as those on the left.

The femoral, popliteal and tibial arteries in both lower extremities have thickened, atheromatous walls, but the lumina are larger than in normal vessels and are nowhere occluded.

**Neck organs:** Not examined.

**Brain:** The dural venous sinuses are not thrombosed. The cerebral leptomeninges are slightly thickened and milky-white over both
convexities of the parietal lobes. The frontal lobe gyri are not atrophic. There is some widening of the sulci in the parietal lobes. Several gyri in the right occipital lobe are a yellow-brown in color and are softened from an old infarct. It is impossible to find an occluded pial vessel responsible for this lesion. In the left occipital lobe region, there is seen a small gray saccular dilatation measuring 5 mm. in greatest diameter, which resembles an aneurysm and is attached to one of the pial vessels. The arteries at the base of the brain are greatly disfigured by many yellow atheromatous plaques. None of the major vessels are occluded. Two small gyri in the right frontal lobe are the seats of old cortical infarction. A considerable portion of the right motor cortex is similarly destroyed. There are no lesions in the basal ganglia. The adjacent parietal lobe gyri have extensive cortical softenings which extend into the subcortical white matter. This process of encephalomalacia reaches its greatest extent in the right occipital lobe. There are no lesions in the brain stem and cerebellum.

A slight degree of internal hydrocephalus affects both lateral ventricles and is the result of an ex-vacuo process. From the tela choroidea of the third ventricle hangs pendant a gray, fleshy, spherical massive tissue, a little less than 1 cm. in diameter and containing a rubbery brown colloid-like material in its center. Its position and appearance vaguely suggest an incipient colloid tumor (Fig. 2 Plate XLII).

Fig. 2. Drawing of transverse section of brain through the third ventricle showing the appearance of the cyst in this cavity. Note also the cortical encephalomalacia in the right parietal lobe.

Microscopic Notes

Thymus: Much of the parenchyma is replaced by adipose tissue but a few islands of lymphoid cells are still visible. There are also present a few Hassall’s corpuscles. The arterioles have greatly thickened, intensely pink staining walls. Beneath the mesothelial covering of the thymus are found a number of fresh petechial and confluent hemorrhages.

Heart: The left ventricular myocardium is replaced in large measure by old dense fibrous scars. Approximately ¼ of the sample of muscle is scarred in this fashion. The scars contain rather large venous channels which are engorged with blood. None of the intramural arterioles are sclerotic. The right ventricular myocardium is likewise scarred but the fibrosis is definitely more focal and less extensive than in the left ventricular wall. Several arterioles are found occluded by what appear to be canalized thrombi. In a number of instances, the muscle is replaced by young granulation tissue in which plasma cells and blood pigment-containing phagocytes abound. The interventricular septum is the seat of massive scarring as well as of acute infarction. The latter lesion is characterized by extensive muscle fiber necrosis and polymorphonuclear leucocytic infiltration. The leucocytes lie between muscle bundles which have lost their striations and are stained intensely red. There is a loss of nuclei and a fragmentation of the muscle bundles. The auricular appendages are filled with recent thrombi. These lie between the interstices of the muscle bundles in the auricular walls. Much of the latter consist of connective tissue replacement of muscle. The loose periauricular adipose tissue is widely infiltrated with leucocytes and is also edematous.

Coronaries: The anterior descending branch of the left coronary artery contains a huge fibrous plaque beneath the intima on one side of the vessel and the lumen is thereby compressed to a mere slit. There are numerous vessels in the atheromatous plaque. The latter has produced a marked pressure atrophy of the media. The middle portion of this branch has literally a pinpoint lumen. The lesion accountable for this is a massive fibrous subintimal scar. The circumflex branch has a lumen which is patent to an estimated 25% of its normal size. This lumen decreased progressively towards the periphery of the vessel and terminally is no larger than a vas vasis”. It is of considerable interest to note that the pathologic process is essentially fibrosis with little of the usual atheroma.
The right coronary artery is similarly affected and its lumen is perhaps patent only to 10% of normal. At the junction of the marginal branch, the vessel lumen is filled with necrotic debris and cholesterol crystals. The intima is disrupted and the grumous material seems to emanate from an atheromatous patch in the wall of the vessel. Beyond the point of origin of the marginal branch, the right coronary artery contains a fresh subintimal hematoma which bulges into the lumen of the vessel and deforms it into a mere semilunar slit. Immediately below this point, the entire lumen is occluded by a fresh thrombus.

**Lungs:** One of the apical pulmonary scars is found consisting of a collagenous connective tissue replacement of the subpleural alveoli. Anthracotic pigment is found within the acellular scar, on the margins of which are present foci of collections of lymphocytes. There is no active tuberculous process. The subpleural scar in the left lung, which is found near the zone of emphysema, consists of a definitely tuberculous focus. A number of multinucleated giant cells are still present within the scar tissue. The latter has the spheroid configuration of a tuberculoma. There is some perivascular and peribronchial anthracosis. Most of the alveoli are filled with fluid and coagulated protein but there is no cellular exudation. Relatively large numbers of dust-bearing phagocytes are also seen in the alveoli. The smaller pulmonary vessels are conspicuous by virtue of their greatly thickened walls, which have narrowed the lumina. The clot which was found in a larger pulmonary artery is distinctly of postmortem origin.

**Spleen:** There is intense acute congestion of the splenic pulp. Otherwise, the spleen is not remarkable except for the enormously hypertrophied arteriolar walls.

**Stomach and Duodenum:** Many microscopic preparations were made of different parts of the stomach, the pylorus and the duodenum. Several sections were taken through the pyloric valve and included the anterior as well as posterior surfaces. The gastric mucosa of the cardia is intact and the gastric glands are of normal depth. Both the chief and oxyphilic cells are well stained. The nodule that was seen in the anterior wall of the pylorus is definitely a leiomyoma. There is no scar in the submucosa or muscle layers nor are any scars demonstrable in the posterior wall of the pylorus. The mucosa of this portion of the alimentary tract is intact. Brunner’s glands are present in the first part of the duodenum beneath an intact mucosa. From these findings it is apparent that no trace remains of the old pyloric ulcer, except for the fibrous adhesion between the gall bladder and the pylorus.

**Pancreas:** Numerous well-formed Langerhans islands are present in the head. The acinar tissue is well preserved and well stained. There is no lipomatosis in this organ.

**Liver:** The sinusoids around the central veins within the liver lobules are atrophic. A few of them are even necrotic and are infiltrated with leucocytes. There is no hemorrhage, however, either in the central vein regions or elsewhere in the liver lobule.

**Adrenals:** The medullary substance is somewhat congested. The zona reticularis contains occasional clumps of necrotic cells. The other cortical zones are not abnormal. There are no hyperplasias or adenomata.

**Kidneys:** The right kidney has the usual number of cortical scars to be expected in a patient of this age. Most of the glomeruli are well preserved and the tubules also are intact. The renal arteries and arterioles are not severely injured by arteriosclerosis. An occasional afferent arteriole has a thickened wall and, when traced into the glomerular tuft, is found to be associated with focal necrosis such as is seen in the malignant form of nephrosclerosis. The picture in the left kidney is quite different. Large areas are found to be necrotic and hemorrhagic. This picture is characteristic of renal infarction.

**Prostate:** The small nodule in the left lateral lobe is seen to be an adenoma. The remainder of this gland presents no unusual features.

**Intestines:** The mucosa of the entire intestinal tract is intact. At frequent intervals, the mucosal vessels are intensely congested and still more infrequently, there are actual hemorhages present. The submucosa is neither edematous nor congested.

**Aorta:** (Fig. 1 Plate XLI). The wall of the aorta just beyond the origin of the left subclavian artery (1) is tremendously thickened on the intimal side by heavy atheromatous deposits. There are rather large, old and fresh hemorrhages in the subintimal atheroma. The latter are chiefly characterized by tremendous numbers of cholesterol crystals. The media is of average thickness but the adventitia is greatly increased in width. The mid-thoracic portion of the aorta (2) has the same histologic appearance. Old blood pigment is very conspicuous in the extensive subintimal plaque which encircles the entire lumen. At the celiac axis (3), the intimal side of the vessel is even more extensively injured than at the higher levels. In one region, the endothelial lining is disrupted at a point where there is much subintimal hemorrhage and a large thrombus clings to the wall. This thrombus is still unorganized and fills only a small portion of the lumen. Two cm. farther along (4), the thrombus, still attached to the intima, has reached such proportions as to fill half the lumen. At the point of origin of the left renal artery (5), the fresh thrombus now fills 2/3 of the lumen of the aorta. Extensive old hemorrhages are seen in the sub-intima of the vessel at this point. The left renal artery is found to be tremendously altered by proliferated and vascularized connective tissue. Below the origin of the inferior mesenteric artery (6), the whole process has changed. Here the entire lumen is filled with an old thrombus containing grumous material and old blood pigment. The hemorrhage in the wall of the aorta fuses with the material filling the lumen. Immediately above the bifurcation of the aorta into the common iliac artery (7), the thrombus which completely fills the lumen is still older. At this point, the intima is not only severely damaged but the media too, is present only in fragments. The left external iliac artery (8)
which is atrophic and has the gross appearance of the internal iliac artery, is nearly completely occluded by what is commonly designated as a recanalized thrombus. The same histologic picture is seen in the right internal and external iliac artery. It is of considerable interest to note that the femoral, popliteal and tibial arteries in both extremities have widely patent lumina. This is true in spite of the rather extensive subintimal atheromatous change in all the vessels.

**Brain:** The lesions in the right motor and occipital regions of the brain are old and distinctly of vascular origin. In addition to the extensive softening in some of the gyri, which has destroyed considerable portions of the cortical architecture, there are also seen many scattered glial scars. One pial artery in the right motor area is found to be completely occluded by an organized thrombus. This vessel, as well as numerous others of arterial and arteriolar size in the meninges and nervous parenchyma proper, are greatly altered by atheromatous change. The subcortex in the zones of infarction contains a condensation of the oligodendroglia, as is often present in cortical injury.

The minute vascular lesion, which is found in the meninges over the left occipital lobe, is revealed on histological examination to consist of a hyalinized hemangioma. There can still be found endothelial-lined channels containing small numbers of red blood cells.

The cystic structure in the third ventricle is filled with a homogeneous colloid. The capsule of a cyst has not been retained in the microscopic preparation. It is doubtful whether this cyst is a genuine ‘colloid cyst.’ It seems more likely that it represents a simple retention cyst of the choroid plexus.

**Final Anatomic Diagnosis**

Generalized arteriosclerosis with especial involvement of aorta, iliac, coronary and cerebral arteries; organized and recent thrombi in aorta (below renal arteries) and iliac arteries; old and recent atherosclerotic and thrombotic occlusions of coronary arteries; scars of myocardium; organized thrombus in pial artery; multiple old cerebral infarcts; cardiac hypertrophy and dilatation; acute left ventricular infarct; thrombus in right atrial appendage.

**Subsidiary Diagnoses:**

- Healed pyloric ulcer.
- Hyalinized hemangioma in the meninges (left occipital lobe).
- Small cyst in the third ventricle of brain.
- Healed apical pulmonary tuberculosis.

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**Glossary:**

- Dr. Arnold Klebs was a Swiss physician who specialized in the study of tuberculosis. He worked with Dr. William Osler at Johns Hopkins University and was a contemporary of Dr. William Welch. He was senior to Dr. Cushing but was his good friend. On his death, he bequeathed his extensive collection of classic books and incunabula to the library in New Haven that also houses the books of Dr. Harvey Cushing and Dr. John Fulton.

- In the letter from Dr. Klebs to Dr. Zimmerman, we come across two interesting words:

  1. **Epos.** This, the dictionary tells us, has two meanings:

     a) **Epic**

    b) A number of poems that treat an epic theme but are not formally united.

     One example of the usage of this word:

     ‘She found her epos in the reform of a religious order.’ Prelude to *Middlemarch* by George Eliot.

  2. **Erlebnis:** experience (event of which one is cognizant)

- Dr. Zimmerman knew in detail about Dr. Cushing’s poor circulation in his toes and the consequent difficulty in walking when he moved to New Haven well before Dr. Cushing died. Dr. Cushing often complained of this to Dr. Zimmerman and for the last year of his life, his chauffer used a wheelchair to take him to his office and home and into and out of his car. Dr. Cushing developed gangrene of his toes. The ischemic symptoms in his lower limbs had made their appearance even when he was at Peter Bent Brigham and Dr. Cushing often told Dr. Zimmerman about how he felt exhausted at the end of an operation and could not stand. He had to sit during most of his later operations. This was one of the reasons why he accepted, with good grace, his retirement from Brigham. The early symptoms had occurred in 1918, while he was with the Harvard Unit of the Expeditionary Force in France during the First World War. He had collapsed during an operation and was hospitalized for about three months.
in France. He was incapacitated for a further six months. He, himself, had diagnosed polynéurite and myélo-radiculite. ‘In retrospect, it was an incorrect diagnosis but all his life he thought that was his major problem. No neurologist or neurosurgeon dare challenge that diagnosis. He had collapsed during an operation. Neuromyelitis does not usually act this way.’ When he developed ischaemic problems in his toes and feet, several eminent internists in Boston and in New Haven diagnosed Buerger’s disease. He was advised to give up smoking.

\(^5\) **Livor mortis**: Discoloration of the dependent parts of the body after death

\(^6\) **Vas vasis**: Another term for vas deferens

\(^7\) **Grumous**: Thick and lumpy as clotting blood. From Latin *grumus*: a little heap.

\(^8\) Reich (1987) disagreed with Dr. Zimmerman’s conclusions. He noted that the features of Cushing’s malady included symmetrical weakness, numbness, and paresthésias of the hands and feet, areflexia, bilateral facial paresis, diplopia, and fever. Neither Cushing nor his physicians were able to make a diagnosis. John Fulton, Cushing’s biographer, misdiagnosed the condition as a ‘vascular polynéurite,’ and Harry Zimmerman, who performed Cushing’s autopsy, incorrectly attributed his symptoms to occlusion of the abdominal aorta. ‘Based on extensive notes in Cushing’s war diary describing the illness, it is readily recognized today as Guillain-Barré syndrome.’