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THE RADICAL SURGERY OF CANCER OF THE LOWER END OF THE COMMON BILE DUCT AND ADJACENT PANCREAS*

BY

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A recent Hunterian Lecture concerned itself, among other problems, with (a) the sphincter arrangements of the terminal portion of the bile duct, and (b) the radical surgery of cancer in that area. The name of Oddi is often associated with the sphincter mechanism in this region, but an Englishman, Francis Glisson, drew attention to the "ostium with the annular fibres" nearly 250 years before the Italian. The description given by either observer was not an accurate one, and there certainly appears to be no valid reason to attach the name of the physiologist from Perugia permanently to this area. To Glisson at least is due the credit of first directing attention to the ostium, and the name of Glisson's sphincter must at any rate appeal to the patriotic.

Cancer of the caruncula major, the head of the pancreas or its duct, or the peripapillary portion of the duodenum is usually loosely designated "ampullary" carcinoma when surgery is undertaken. Although many cases in the literature purport to be examples of primary carcinoma of the "ampulla," true ampullary cancer must be rare, since this anatomical abnormality is itself infrequent. However, Lieber, Stewart, and Lund (1939) describe an undoubted case: a patient died of obstructive jaundice due to a small polyp arising from the mucosa of a definite ampulla. The new growth infiltrated the surrounding pancreas and muscular wall of the duodenum, but did not implicate the surface epithelium of the intestinal mucous membrane or of the choledochus or pancreatic duct. The specimen was regarded by the Boston surgical authors as an undoubted example of primary cancer of the ampulla.

Lieber, Stewart, and Lund (1939) in their industrious survey of cancer of this area were able to collect only three definite cases of primary carcinoma of the duodenal mucosa covering the caruncula major; the cases had previously been reported by Borelius, Le Noir and Courcoux, and by Countryman. They collected three cases of primary carcinoma of the terminal portion of Wirsung's duct in the literature—those of Letulle and Verliac, of Carnot and Harvier, and of Hadfield.

A very large number of cases of so-called "ampullary" cancer belong to an indeterminate group in which all the epithelial structures of the "papilla" are involved. This early implication of adjacent tissues depends more on the proximity of anatomical structures than upon any special malignancy of the tumour. Such tumours are rarely larger than a hazel-nut, and are said to be limited to the "papilla" in 74% of the patients.

Surgical literature relating to cancer of this region always emphasizes the slow growth and low-grade malignancy of many of the tumours (Outerbridge, etc.). Even in cases in which clinical evidence exists that a carcinoma of the head of the pancreas implicating the bile duct has been present for

some time and attained considerable magnitude, mobility of the tumour may still be retained and surgical removal be practicable. In one case of my own, for which three palliative operations (!) of diverse nature had already been performed at another institution during the previous fifteen months and in which the diameter of the tumour was nearly 3½ in., the affected portion of the head of the pancreas was found at necropsy still to retain mobility and showed no involvement of the portal vein or its parent tributaries, and there were no metastases. The hope had been entertained that despite the regrettable wastage of time a radical operation might yet prove possible, but the woman unfortunately succumbed from a mishap during a very minor preliminary operative procedure.

More recently, J. C. Dick (1939) has stressed the low malignancy and the slight tendency to early dissemination exhibited by tumours of the lowermost end of the common bile duct; in 11 out of 13 cases at necropsy he found no extension of the tumour beyond the wall of the choledochus, and no secondary growths were demonstrable in glands or other organs. Microscopically, these tumours of the lowermost end of the common duct are adenocarcinomata, composed of irregular acini with large well-formed columnar cells; the cells stain darkly and have well-formed nuclei. There is little evidence of anaplasia, and very few mitotic figures are discernible. The tumour may be a small round, firm, whitish growth of the size of a cherry-stone; it may assume the form of multiple soft vegetations, varying in size from a pea to a hazel-nut. At other times the growth is a diffuse stenosing type, perhaps 1 to 2 cm. long and extending into the head of the pancreas.

Two illustrious American surgeons were the first to perform a resection of the "ampulla." To Halsted (1899) belongs the credit of being the pioneer in 1898, although his patients lived for only nine months after operation; William Mayo (1909) performed the second successful removal of an ampullary cancer in 1900, his patient surviving two years.

The end-results of even minor radical surgery for cancer of the caruncula major are naturally more hopeful than those of palliative measures. Of 7 patients submitted to transduodenal resection at the Mayo Clinic 5 recovered, and the average post-operative survival was nearly 26 months, whereas prospective survival after palliative measures amounted to only 14 months. The numbers of radical operations of varying degree for cancer of this region have slowly and steadily increased, so that Whipple, Parsons, and Mullins (1935) were able to report 80 cases of resection, mostly of limited scope.

Nevertheless, even after limited transduodenal removal some remarkably prolonged survivals have been reported: thus Körte's patient was alive and well 22 years after a transduodenal resection of an ampullary carcinoma; and Schloffer's cases, reported by Clar of Prague, survived 15 years. Kelly's patient was well 9 years after operation, and Cabot's survived 8 years. Lewis had a case of 8½ years' survival, and Oehler had one of 6 years' good health; Lauwers had two successful cases, one surviving 4 years.

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Involvement of the surrounding pancreas and adjacent tissues demands an increased range of operation if extirpation is to be effective for the more extensive and infiltrative lesions. The value of the two-stage operation in cases of prolonged jaundice has now been learned, and the pre-operative measures directed towards the improvement of liver function and the control of haemorrhage have emboldened surgical effort; experimental work has demonstrated that the external secretion of the pancreas is no longer to be reckoned as indispensable in the digestive economy. The pioneer work of Allen Whipple and his colleagues at the Presbyterian Hospital, New York, demonstrated incontrovertibly the possibility of a truly radical operation for cancer of the "ampullary" region, and the successful results of subsequent operations by these pioneers and by some few other surgeons on each side of the Atlantic have put the operation upon the surgical map. Although the first success to attend a "radical" removal of cancer of the pancreas occurred in 1935, Maingot (1941) states that up to December, 1941, there had been published only 15 radical two-stage resections; including the second part of the duodenum, a variable amount of the head of the pancreas, and even the neck of that organ. Five of these 15 patients died almost outright from the operation; in another promising case (Illingworth, 1939) death occurred from biliary peritonitis more than 6 weeks after operation; two patients died at later dates from the effects of contraction of the surgical stoma between the biliary tract and digestive tube, and three developed subsequent metastases. Thus of the 15 recorded cases collected by Maingot (1941) in only 4 instances were the patients alive at the time of publication of that author's paper.

This Hunterian Lecture affords me the opportunity of adding some personal cases in which at least immediate success has attended limited transduodenal and transcholedochal removal and the more radical extirpation performed according to the Whipple technique; some cases have enjoyed a more prolonged survival. I also include one or two published and some hitherto unpublished cases belonging to my surgical friends.

Transduodenal Resection (2 Personal Cases)

A few years ago, in a discussion at the Meeting of the Association of Surgeons of Great Britain and Ireland held in London, I made mention of two successful cases, in which very early in my surgical career I performed transduodenal resection of a small malignant tumour of the *caruncula major*. In the course of operations upon two jaundiced patients the tumour felt through the duodenal wall was erroneously thought to be an irremovably impacted calculus, and the duodenal segment of the bile duct was therefore approached through the gut. In each case the tumour was only crudely removed by means of a curved pair of scissors, and the anterior wall of the duodenum sutured; each of the tumours was reported as a short columnar-celled carcinoma.

In the *first case* of the two, the patient, a woman of about 50, operated upon as far back as 1909, died of jaundice and palpable liver metastases two and a half years later, leaving no doubt as to the accuracy of the pathological report.

The *second patient*, treated in a similar amateur fashion, operated upon in 1911, was alive at the beginning of the last war, in 1914, but she was then lost sight of; three years of freedom from recurrence had elapsed since her operation.

Transcholedochal Removal of Tumours of Lower End of Common Bile Duct

Case 3.—A lady aged 55 was operated upon for persistent painless jaundice in 1925. Exploration of a greatly distended common duct revealed several small papillomatous outgrowths within the duct and a larger more sessile tumour obstructing the lumen of the canal almost at its lowermost end. This terminal portion of the duct was exposed and opened by a retroduodenal approach; the tumours were removed locally, the patency of the ostium and permeability of the duct demonstrated, and both openings in the choledochus closed. An anastomosis was effected between gall-bladder and stomach; a drain was left in Morison's pouch. Despite a favourable histological report, signs of pyloric obstruction supervened some months later, necessitating a palliative gastro-jejunostomy. A mass was present in the head of the pancreas which left little doubt as to its nature. The patient died about a year after the primary intervention with all the evidences of malignancy in the abdomen.

Radical Excision of "Ampulla" with Part of Duodenum and Pancreas

Case 4 (Fig. 1): Man aged 60; Painless Jaundice 5 Weeks; Distended Gall-bladder; Ampullary Carcinoma; Death.—Cholecysto-gastrostomy; gastro-jejunostomy; division of first

FIG. 1

part of duodenum; radical removal with reimplantation of ducts. Most unwisely this operation was performed in one stage; oliguria and subsequently anuria developed, and death ensued in 5 days. The suture lines were in satisfactory condition.

Case 5: Man aged 58; 9 Weeks' Painless Jaundice; Distended Gall-bladder; Operation June, 1939; Ampullary Carcinoma.—*First operation:* Small bowel divided and united En-Y. Anastomosis between distended gall-bladder and short limb of Y-shaped jejunal junction. *Second operation:* Six weeks later a posterior gastro-jejunostomy was performed, care being taken that the apposed jejunal coil was distal to that segment of bowel with which the gall-bladder was connected, lest an anastomotic ulcer should result. The duodenum was divided and the gastric end inverted; the commencement of the third portion was similarly treated, and the descending duodenum and adjacent pancreas were removed, the common bile duct and pancreatic duct being each ligated with silk. The extraperitoneal bare area was drained. The patient recovered, but died in 6 months from hepatic metastases.

Case 6 (Fig. 2): Woman over 60; Painless Jaundice nearly 3 Months; Modern Pre-operative Therapy; Operation, 1940; Two-stage Intervention; Ampullary Carcinoma.—*First operation:* Cholecysto-gastrostomy. *Second operation:* Six weeks

FIG. 2

later, posterior gastro-jejunostomy. Removal of descending duodenum with adjacent head of pancreas. Common bile duct and pancreatic duct ligated with silk. Drainage of bare retroperitoneal space. Pancreatic juice leaked in small quantities for several weeks; ultimately ceased. Patient is well 1 year and 9 months later.

Case 7: I have previously recorded a successful excision of a carcinoma of the *body of the pancreas* (Gordon-Taylor, 1934). At the operation, performed in July, 1927, a mass was removed one and a half times the size of the closed fist. The tumour was reported upon by Prof. S. Baker, now of Manchester University, as a columnar-celled carcinoma; an enlarged lymphatic gland attached to the mass was not infected with growth. The splenic artery required wide excision since it was implicated in the tumour mass; in addition to the removal of a length of the upper circumference of the expanded splenic vein, the left half of the commencement of the portal vein also required ablation. The operation was laborious, and at its

termination only that part of the pancreas embraced by the concavity of the duodenum appeared to remain. No subsequent sequela referable to the spleen made me regret the decision to conserve that organ, despite the surgical interference with both its arterial and its venous blood supply. The patient continued in excellent health until the autumn of 1938—that is, 11 years—when the possibility of a recurrence suggested itself. *Just over 13 years after the removal of the tumour* he died from undoubted abdominal malignancy—probably a late metastasis of the original tumour.

Case 8: A Calcified Mass embedded in the Pancreas and compressing the Common Bile Duct; Removal of Mass together with Portion of Head of Pancreas.—A stoker 49 years of age with jaundice of 4 months' duration; rather poor physique. Two-stage operation after modern pre-operative measures. *Cholecysto-gastrostomy*; at operation a firm mass was palpated in the head of the pancreas near the ampulla, and was regarded as confirmatory of the accuracy of the pre-operative diagnosis of ampullary cancer. *Second operation*, undertaken 6 weeks later: The second part of the duodenum was mobilized and the mass approached from behind. The tumour was found embedded in the substance of the head of the pancreas in intimate proximity to the retroduodenal and pancreatic portion of the common duct, and was removed from the pancreas with some of the gland tissue. On section the tumour was found to consist largely of calcareous material, possibly a mass of agminated calcified tuberculous glands. There was perhaps some justification for the mistake in diagnosis, but at least the patient is to be congratulated on the pathological nature of the compressing mechanism, which before this experience I might have seriously doubted.

Prof. C. F. W. Illingworth has had two admirable unpublished cases in which a successful radical two-stage operation for cancer of the pancreatic head was performed, and which I had the good fortune to see in Glasgow some months ago. My friend Victor Hurley of Melbourne told me that he had successfully removed a malignant tumour from the head of the pancreas by a retroduodenal approach, without removing the duodenum or bile duct. Rodney Maingot's (1941) excellent case is the first truly radical and successful case to be reported in Britain.

Some new growths of the ampullary region are apparently radiosensitive. Upcott (1935) performed a local excision of an ampullary growth and introduced radium on a probe down the common duct; the patient was well *15 years later*. Sampson Handley (quoted by Upcott, 1935), employing 6 mg. of radium for 5 days, was able to report 3 cases free from recurrences for 10 months, 2 years, and *14 years*, respectively. Sir James Walton (1939a) reported two successful cases of resection of the common bile duct for cancer in his Bradshaw Lecture of 1939, but amid the wealth of surgical experience and skill contained in this address these two cases deserve special mention lest they escape notice. Mr. C. E. Kindersley of Bath had also a successful case of resection of the junction of the cystic and common bile duct; this patient has survived several years.

Of *transduodenal resection of the duodenal end* of the common bile duct, my friend Mr. David Ligat of Hastings, operating at Middlesex Hospital in 1916 during the last war, had a successful case, the patient living *nearly five years* before ultimately dying of obvious malignant recurrence in the liver. This man had been jaundiced for 4 or 5 months, and the extrahepatic ducts were enormous.

These cases have been reported in the hope that the younger generation of surgeons may be encouraged to attempt to cure and not merely to palliate. The natural history of ampullary and pancreatic tumours justifies more vigorous surgical effort, and the end-results of the cancer surgery of this region should compensate the operator for his enterprise.

The concluding part of the Lecture will appear, with a list of references, in next week's issue.

The plan for fusion recommended by the Council of the Incorporated Association of Hospital Officers and of the Incorporated Association of Clerks and Stewards of Mental Hospitals has been adopted by extraordinary general meetings of both associations. Accordingly, from Oct. 1 next the two bodies will be amalgamated under the title of the Incorporated Association of Hospital Administrators, and membership will be open to all duly qualified lay hospital administrators.

DIPHTHERIA IMMUNIZATION OF ADULTS

BY

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The admirable paper by Fulton *et al.* (1942) has, with convincing proof, laid down a highly efficient routine for the immunization of children with alum-precipitated toxoid (A.P.T.). The dosage of 0.2 c.cm. followed by a second dose of 0.5 c.cm. at an interval of not less than 4 weeks has received the approval of the Chief Medical Officer to the Ministry of Health in his letter to all medical officers of health dated May 8, 1942. It is safe to assume that such a method will become routine and will at last lead to satisfactory immunization in this country. Provided we can rely on the antigen, the checking of which is the concern of the issuing and controlling laboratories, we now have an efficient and simplified diphtheria prophylaxis. Schick-testing can be dispensed with and records can be reduced to the insertion of a batch number and two dates upon a card. Whether this work be done in a consulting-room, a child welfare clinic, or a school will matter little. The aim now should be to get over 80% of children under 10 years of age treated in this manner.

At the same time the Chief Medical Officer to the Ministry, in another letter, advised that nurses in general hospitals who are Schick-positive should be immunized with toxoid-antitoxin floccules (T.A.F.), 3 doses of 1 c.cm. being injected at intervals of 3 weeks. The reason given for this recommendation is that T.A.F. tends to give rise to less reaction than does A.P.T.

Fulton *et al.* in their paper state that above the age of 18 years the number of subjects tested (20) was too small to enable them to obtain a reliable figure for the Schick-conversion rate. This encourages me to add as a small contribution the figures I have collected during the past 9 years in the course of immunizing the staff at the Hull City Hospital. Though not large they have been carefully compiled, and all testing, readings, and injections have been done personally. All persons in the group are more than 16 years of age, and the great majority between 18 and 20. Most are nursing and domestic staff at the hospital, but occasional visitors, medical and otherwise, have been included.

After various experiences with other antigens since 1922, including T.A.M. and F.T., I began to use T.A.F. in 1933, giving 3 injections at monthly intervals and Schick-retesting 4 weeks after the last dose. The Schick-conversion rate was not good, and largely for this reason I turned to A.P.T. in March, 1935, giving 0.3 c.cm., followed after 4 weeks or a little longer by 0.3 c.cm., with a Schick-retest one month later. Originally I had intended to give 0.25 c.cm. and 0.25 c.cm., but there was always enough in a 0.5-c.cm. ampoule to give two doses of 0.3 c.cm. to two subjects, so it seemed a pity to waste antigen. The Schick-conversion rate rose to 100%. I get no severe reactions, and the method, except for an increase to 0.5 c.cm. for both doses in 1940, has been in use since. In 1936 I began to give a single dose of 0.3 c.cm. of A.P.T. to Schick-negative reactors if they did not have a pseudo-reaction, and have continued that procedure, increasing the dose to 0.5 c.cm. in 1940. The results are summarized in Table I. The details given in this Table suggest that the T.A.F. used in 1933 was a weak antigen and that it was considerably improved in the following year. Despite this improvement, the T.A.F. results as a whole were poor (Schick-conversion rate 78%). The excellent results with A.P.T. were so soon apparent that there was no question of return to the older antigen. I would regard any such return as a regression.

Reactions

There were no severe reactions in any of the 388 adults immunized. I have notes of only 5 moderate local reactions—4 with A.P.T. and 1 with T.A.F. One of the 4 A.P.T. reactors was a pseudo-negative who was given 0.1 c.cm. of A.P.T. as a detector dose. Some local reactions have doubtless