

potency of sulfonylureas in diabetics can be predicted from acute hypoglycemic potency in normals and metabolic half-life. If this is true, then it should be possible to predict half-life from potency in normals and diabetics. Since U-17835 has been found (relative to tolbutamide) to be about as potent acutely in normals as it is clinically in diabetics, it suggests that U-17835 may prove to have a half-life similar to that of tolbutamide.

Although U-17835 may have a half-life similar to tolbutamide, it should be emphasized that duration of action and/or potency can be affected by rates of intestinal absorption. This is supported by observations in other areas of biological activity where pharmaceutical alterations of absorption rates can result in maintenance of effective blood drug levels and increased duration of action (10, 11).

Although U-17835 has a greater potency in man than tolbutamide, extensive clinical trial will be necessary to establish the significance of these findings with U-17835 regarding increased efficacy or fewer side effects compared to tolbutamide.

Summary. U-17835 ([N-(1-hexahydro-1-azepinyl)-N'-p-tolyl-sulfonylurea]), a new blood sugar lowering sulfonylurea, was 4-6 times more active than tolbutamide in intact rats and 4 times more active in adrenalectomized rats. At equipotent doses it was not longer acting than tolbutamide in intact rats.

Normal human subjects showed U-17835 to be 6-7 times more effective than tolbutamide in lowering blood sugar after a single dose. In 3 diabetic patients, U-17835, given for 8 weeks, was found to be 5-10 times more active than tolbutamide, and it showed no signs of intolerance. This compound was also better tolerated than tolbutamide in both rats and mice.

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Special Tubes for Total Bile and Pancreatic Juice Collection in the Human.* (26592)

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Soft rubber and plastic tubes were designed, which, when implanted in the post-operative wound in patients operated on for biliary and pancreatic disease, permitted physiologically significant measurements of total

human bile and pancreatic juice. The rubber tube for bile collection[†] was constructed like a T-tube, but the long arm was composed of 2 tubes, one draining the liver, the other connected to the lower limb, which was of small

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† These tubes were manufactured by C. R. Bard, Inc., Summit, N. J.

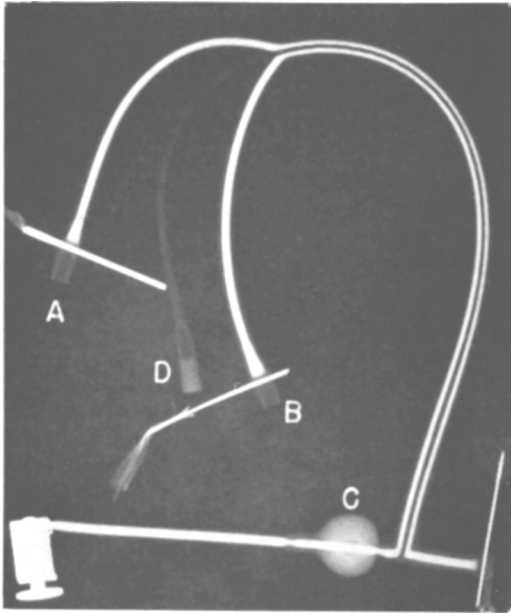


FIG. 1. Special T-tube for total bile collection: X-ray study of Urokon-filled tube to demonstrate its internal structure. Proximal tube (A), distal tube (B), balloon (C), and self-sealing tube to fill balloon (D).

diameter, and extended into the duodenum. Encircling the lower limb was an enlarged, soft balloon which could be inflated with water through a fine tube incorporated into the long arm of the T-tube. This tube was inserted into the common duct in the same manner as an ordinary T-tube. As all studied patients had the sphincter of Oddi sectioned, no hazard was created by the transampullary indwelling tube.

The plastic tube for total collection of pancreatic juice[†] had a double lumen, a larger lumen draining the pancreatic duct, a finer lumen connected to 2 balloons. One small balloon encircled the terminal end of the tube in the duct of Wirsung, and the other larger balloon was attached at the outside end. The sealed balloons and connecting tube were filled with water, so that compression of the larger accessible outside balloon distended the smaller indwelling balloon. The technic of intubation of the pancreatic duct was described previously (1).

Bile was collected in a plastic bag attached to the proximal tube, and pancreatic juice in a plastic bottle immersed in an ice-filled ther-

mos bowl. Volumes were recorded every 2 hours, a small aliquot kept for analysis, and the rest of the bile or pancreatic juice returned to the patient either through the distal arm of the biliary tube or through a gastrostomy tube if the biliary tract was not drained.

After the tubes described here were perfected, 238 24-hour collections of bile were made on 22 patients, and 75 24-hour collections of pancreatic juice were made on 38 patients. Total collections were started about 12 days after operation, when the patients were up and around and eating 3 regular meals a day. The tubes were tolerated without complaint and removed at will when the experiments were concluded. There were no untoward effects. Occasionally the pancreatic tube slipped out into the duodenum, terminating the collection of pancreatic juice.

The analyses of these juices, and the effect of disease, diet and drugs will be reported elsewhere. However, as indication of the effectiveness of these tubes, it is of interest to note that the 24-hour volume of bile from apparently normal livers, varied from 1000-2000 ml and that the 24-hour volume of pancreatic juice from apparently normal pancreas, varied from 1500-4000 ml in different individuals.

Discussion. The special biliary tube is unique in its application to the biliary tract, in that not only is the total secreted bile collected but also all the bile can be returned to the patient's duodenum at will. Thus, bile

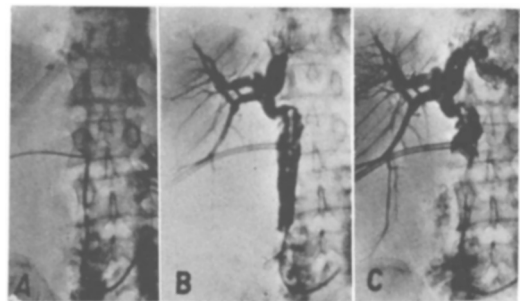


FIG. 2. Special T-tube after insertion into patient: (A) Distal tube entering duodenum, filled with contrast solution; (B) proximal tube is inj., contrast solution filling biliary tract and running around distal tube into duodenum; (C) balloon blown up, showing complete obstruction of common duct.

salts are reabsorbed, and recirculate in the physiological enterohepatic pattern. When total secreted bile is collected and not reinjected, measured secretion is found to average 400-500 ml. Under such abnormal conditions bile salts are not reabsorbed from the intestinal tract for reutilization. The liver has to manufacture bile salts each day anew. On the basis of physiological collection of bile as described here, the daily normal volume of biliary secretion in man varies between 1000 and 2000 ml. These figures are at variance with those suggested in text books of physiology, about 500 ml(2).

Total collection of human pancreatic juice is possible only if there is no functioning accessory duct of Santorini. That there is no such accessory duct can be ascertained by performing a pancreatogram either at operation, or in the post-operative period(3). Daily measured volumes of pancreatic juice

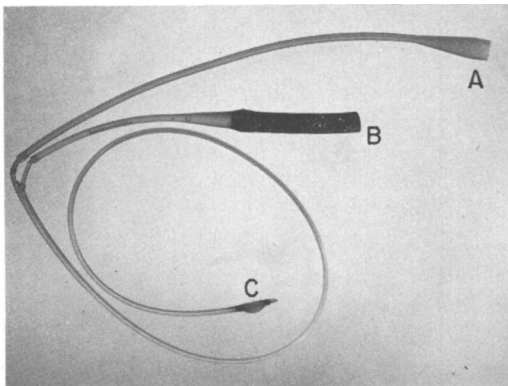


FIG. 6. Special tube for total pancreatic juice collection: Collection tube (A); sealed rubber tube end (B) of fine tube connected with tiny balloon (C), encircling end of collecting tube. Compression of rubber end causes distention of balloon, after it is inserted in terminal end of duct of Wirsung.

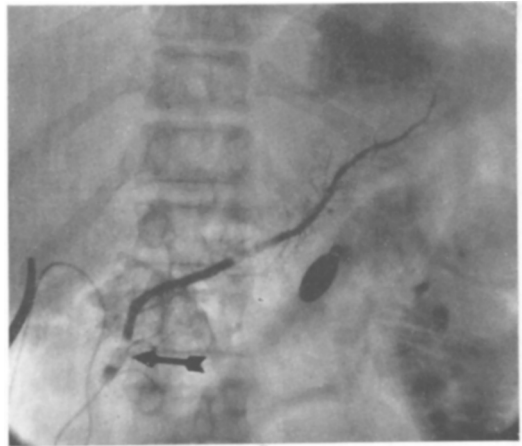


FIG. 4. Special tube for pancreatic juice collection after insertion into patient: Pancreatogram visualizes whole pancreatic duct, and outlines distended balloon (arrow).

secretion in man (1500-4000 ml) are at variance with the usual given figure of 700 ml mentioned in publications(4). Our figures were obtained from patients in whom the pancreas, from clinical evidence and by direct observation at operation, was normal.

Summary. Special tubes for measuring total output of bile and pancreatic juice in man under physiological conditions, are described. Bile secretion from normal livers varied between 1000 and 2000 ml; pancreatic juice from normal pancreas varied between 1500 and 4000 ml.

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