

tion of streptomycin and PAS, such an exacerbation will be avoided. A progress report, together with results of this form of combined therapy in other cases, will form the basis of a subsequent communication.

It is of interest to theorize as to the cause of the sudden deterioration of this patient's condition immediately prior to the institution of cortisone treatment. There is published evidence, again substantiated by our own experience, that untoward reactions have been encountered following the intrathecal instillation of both streptomycin<sup>11</sup> and streptokinase-streptodornase.<sup>4</sup> Any form of therapy, therefore, which renders unnecessary the intrathecal administration of either agent would appear to constitute an important therapeutic advance.

#### PROGRESS NOTE

A progress note in April, 1952 shows the patient to be in good health, with no x-ray evidence of pulmonary tuberculosis. Cisternal punctures are within normal limits, except for 10 to 20 W.B.C. Lumbar punctures also show 34 W.B.C., with 280 mgm. of protein and 680 mgm. of chloride.

#### SUMMARY

1. A case of tuberculous meningitis is reported in which the addition of cortisone to the

streptomycin regimen resulted in dramatic and continued improvement in both the clinical condition and the cerebrospinal fluid findings.

2. The partial resolution of an established intrathecal block was apparently accomplished by this treatment.

3. The theoretical considerations underlying the administration of cortisone in tuberculous meningitis are discussed.

NOTE.—In a "Morning Lecture" entitled, "The Clinical Application of Pituitary Adrenocorticotrophic and Adrenal Steroid Hormones," delivered at the 1951 Annual Meeting of the American College of Physicians, and later published (*Ann. Int. Med.*, 35: 615, 1951), Dr. Laurance W. Kinsell briefly outlined his experiences in two cases of tuberculous meningitis treated with ACTH. These experiences appear to be quite similar to ours with cortisone.

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## AN ARTIFICIAL BILE DUCT\*

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A SEARCH OF THE LITERATURE concerning transplantation of skin revealed no record of its application in the reconstruction of tubular structures within the abdomen. In view of the success of MacLean and Gerrie<sup>1</sup> in the replacement of portions of the male urethra by split thickness grafts it seemed reasonable to suppose that skin might be so used, especially in the reconstruction of portions of the biliary tract. Our preliminary report<sup>2</sup> covers the earliest results of this experiment.

Several investigators have studied the fate of buried skin for periods of several years. Peer and Paddock<sup>3</sup> examined specimens of skin buried

subcutaneously at intervals of one week to one year. Mair<sup>4</sup> used whole thickness skin grafts in the repair of herniæ in man and studied specimens excised at various intervals after implantation. Uihlein<sup>5</sup> described tissue from an area where skin had been used four years previously in the repair of a hernia. The above reports, concerning the fate of buried skin, include observations which differ from one another although the conditions under which they were made were similar. Mair and Uihlein noted eventual metaplasia of buried skin, whereas Peer and Paddock recorded survival of skin elements over equally prolonged periods. These reports agree, however, in one important respect, that buried skin heals on its dermal aspect to the tissue bed in which it is implanted and acquires a rich vascular supply.

Price and Lee<sup>6</sup> planted free full thickness skin grafts on the anterior serosal surface of the stomach and on the parietal peritoneum near the stomach. Later they implanted these grafts, with their new blood supply intact, in windows in the

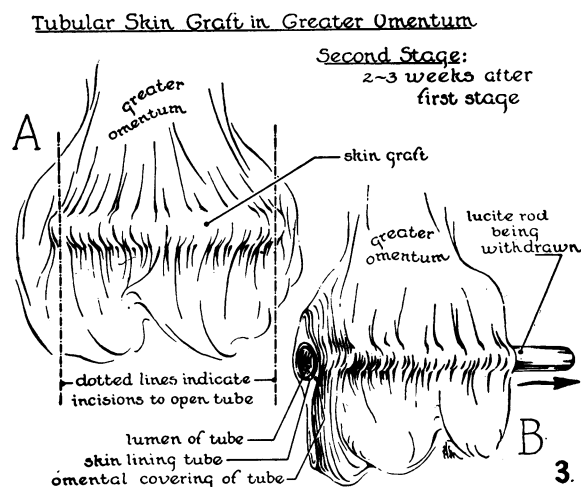
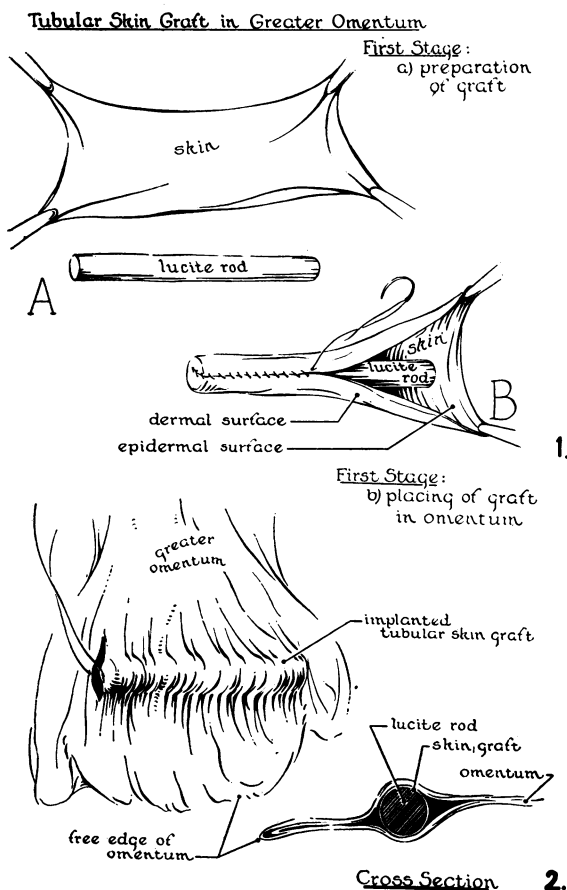
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stomach and observed the effect of gastric digestion upon them. Partial digestion occurred, but islands of residual epithelium could be found histologically after two months. This finding indicates that skin has some degree of resistance to the corrosive and digestive action of gastric juice. It is felt that this resistance of the skin was due to the fact that it had a good blood supply, for free skin placed in the stomach is digested.

The following report is confined to a description of experiments in which skin-lined tubes in the greater omentum were used to conduct bile

In order to construct a tube, a rectangular skin graft was sutured about a lucite rod with the epidermal surface next the rod and the dermal surface exposed (Fig. 1). The tubular graft, with its lucite splint, was then embedded in the greater omentum through a small incision in one of its layers. The delicate omentum adhered readily to the dermis of the graft (Fig. 2). Specimens were recovered at intervals of 11 to 34 days after implantation.

B. *Conduction of bile by means of skin-lined tubes in the greater omentum.*—Second stage operations were performed upon one rabbit and a number of dogs to test the function of the preformed, skin-lined tubes in conducting bile. In general, this operation was carried out between two and three weeks after the first stage.



from various points in the biliary tract into either the duodenum or jejunum.

**METHODS**

The dependent edge of the greater omentum was chosen as a bed for the grafts because of two important characteristics, rich vascularity and free mobility. Anastomoses of the skin-lined tubes to hollow viscera were carried out in two layers, mucocutaneous and sero-seromuscular.

A. *Implantation of tubular skin grafts in the greater omentum.*—Rabbits and dogs were used. All operations were performed with general anaesthesia and aseptic technique.

The tube was prepared by amputating each closed end to expose the lucite rod splint. The rod was then removed and the lumen of the tube flushed out with saline solution to remove accumulated desquamated debris (Fig. 3). In small animals the tube was anastomosed to the gall bladder at one end and to either duodenum or jejunum at the other. The common bile duct was then doubly ligated and divided, to ensure passage of all the bile through the skin-lined tube. In larger dogs, with larger bile ducts, the common duct was divided just distal to the origin of the cystic duct and its distal end ligated. The proximal end was then anastomosed to one end of the skin-lined tube. The other end of the tube was anastomosed to either duodenum or jejunum.

These animals were observed for varying periods of time before being sacrificed for examination of the parts involved.

RESULTS

In Table I is shown a summary of the experiments. The last column describes briefly the result in each experiment and its duration from the time of the second stage operation. In twelve experiments (4 rabbits and 8 dogs), in which implantation of a tubular skin graft in the greater omentum was carried out, the skin survived, became firmly healed in its omental bed and did not give rise to gross infection.

Fig. 4 is a photomicrograph showing a section of the wall of the tube 34 days after implanta-

tion to be intact and patent, without leakage of bile into the peritoneal cavity. Rabbit No. 3 and dog No. 7 died of pneumonia, dog No. 3 died of the effects of an anæsthetic, and dog No. 9 of an abdominal wound infection (Table I). The periods of survival after the second stage operation in these four instances were too short to provide useful information regarding the fate of skin-lined tubes conducting bile.

The tube of dog No. 1, examined 20 days after implantation of the full thickness graft, showed patchy areas of loss of epidermis although all

TABLE I.

EXPERIMENTAL USE OF A SKIN-LINED TUBE IN THE GREATER OMENTUM					
<i>Rabbits</i>					
No.	<i>1st stage</i>	<i>2nd stage</i>	<i>Interval</i>	<i>Type of op.</i>	<i>Results</i>
1	Dec. 11/47	Jan. 14/48	34 days	Biopsy	Healthy, skin-lined tube.
2	Feb. 6/48	Feb. 23/48	17	Biopsy	Healthy, skin-lined tube.
3	Feb. 18/48	March 12/48	23	Gall bladder to jejunum	Died of pneumonia on 2nd day, anastomoses intact.
4	March 9/48	March 20/48	11	Biopsy	Healthy, skin-lined tube.
<i>Dogs</i>					
1	March 17/48	April 6/48	20	Gall bladder to jejunum	Sacrificed at 28 days; wound infection; partial biliary obstruction.
2	April 12/48	May 3/48	21	Bile duct to duodenum (2nd part)	Sacrificed at 55 days; wound infection; incomplete biliary obstruction.
3	April 19/48	May 5/48	16	Gall bladder to jejunum	Died on 1st day, of the effects of the anæsthetic.
4	_____	_____	_____	_____	Anæsthetic death at first stage operation.
5	April 30/48	May 19/48	20	Bile duct to duodenum (1st part)	Sacrificed at 215 days. Normal serum bilirubin throughout. Bile duct epithelium lining tube. Cirrhosis of liver. No biliary stasis.
6	May 26/48	June 10/48	15	Gall bladder to jejunum	Sacrificed at 193 days. Normal serum bilirubin throughout. Epidermis lining tube. Very mild cirrhosis of liver. No biliary stasis.
7	June 1/48	June 17/48	16	Gall bladder to jejunum	Died of pneumonia on 9th day. Anastomosis intact and patent.
8	June 4/48	June 22/48	18	Gall bladder to jejunum	Sacrificed at 246 days. Normal serum bilirubin throughout. Epidermis lining tube. Mild cirrhosis of liver. No biliary stasis.
9	June 8/48	June 23/48	15	Gall bladder to jejunum	Died of abdominal wound infection with abscess on 4th day. Anastomoses intact and patent.

tion of the graft in the greater omentum of a rabbit (rabbit No. 1). Marked vascularity of the dermis is obvious. The epidermis has survived and there is no evidence of inflammation.<sup>2</sup> Figs. 5 and 6 show sections of the tubes of dogs 5 and 6 at the time of the second stage operation. They exhibit essentially the same features as those demonstrated in Fig. 4.

In one rabbit and eight dogs the tube was used to conduct bile in one or other of the manners described (Table I). Rabbit No. 3 and dogs No. 3, 7 and 9 died 2, 1½, 9 and 4 days, respectively, after the second stage operation. In all of these, postmortem examination showed the anastomoses

the dermis had survived (Fig. 7). Following the first operation there was a rather severe wound infection and this had extended into adhesions between the wound and the greater omentum covering the tube. A moderate degree of fibrosis had developed in the areas adjacent to the inflammatory process. This animal developed slight jaundice on the 24th day and was sacrificed 28 days after the second stage operation. The diameter of the tube was found to have decreased from 4 to 2 mm. during the 28-day period in which it conducted bile from the gall bladder to the jejunum. Considerable epidermal regeneration had occurred in spite of continued exposure

to bile (Fig. 8). Several small concretions were adherent to exposed silk sutures at the jejunal end of the tube.

Although healing eventually occurred, severe abdominal wound infections followed both operations upon dog No. 2. It was technically very difficult to anastomose the tube to the tiny bile duct (diameter 4 mm.). Jaundice appeared on the 21st day and serum bilirubin levels at intervals indicated progressive biliary obstruction. This was confirmed at autopsy after sacrifice of the animal on the 55th day. The tubal lumen was approximately 3 mm. in diameter, except at its ends where zones of scar tissue were present, causing further constriction.

Three experiments (dogs Nos. 5, 6 and 8) are of greater importance because of the long

and a partial epidermal lining at the intestinal orifice of the tube where a few hair follicles remained. The tube was lined chiefly by *biliary duct-epithelium*. There was a mild chronic exudative inflammatory process, which was also seen in the wall of the cystic duct and gall bladder. Pericholangitis was absent.

Microscopic examination of the artificial bile ducts of dogs Nos. 6 and 8 revealed essentially the same features (Fig. 10). These ducts retained a well-preserved epidermal lining and thick collagenous wall in which were hair follicles, sebaceous and apocrine sweat glands together with bundles of smooth muscle. There was some inflammatory reaction in and beneath the duct lining, and a mild intrahepatic pericholangitis and fibrosis without biliary stasis.

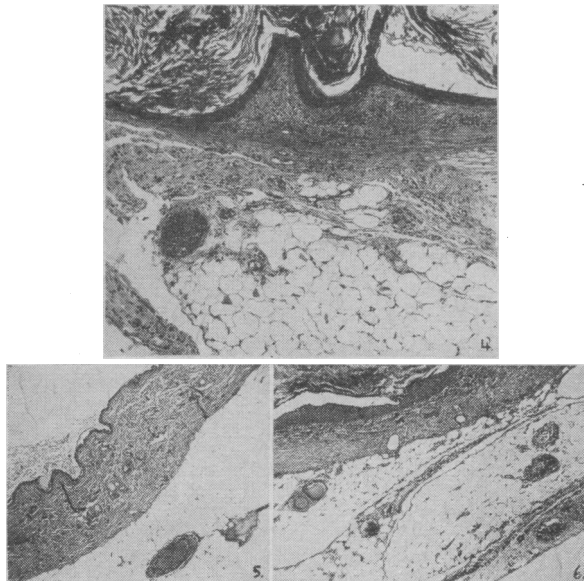
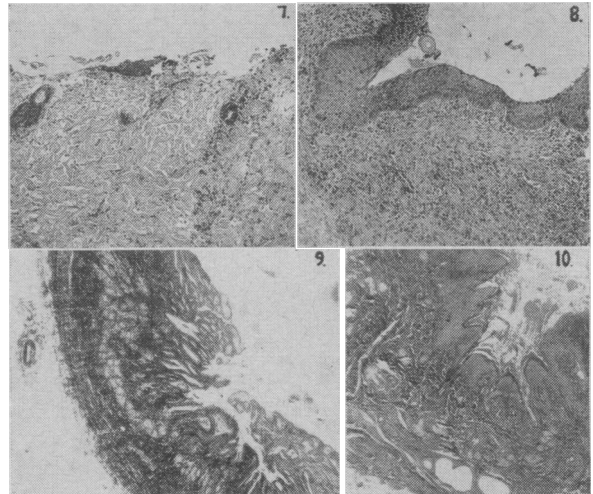


Fig. 4.—Tubular, split thickness skin graft 34 days after implantation in the greater omentum of Rabbit No. 1. Note vascularity of the dermis, absence of inflammatory reaction and survival of epidermis. Figs. 5 and 6.—Show essentially the same features.

periods during which they were observed. Wound infection did not complicate these cases, and biliary obstruction was excluded by monthly serum bilirubin determinations and postmortem examination of the ultimately sacrificed animals. All three developed a mild degree of cirrhosis of the liver but no biliary stasis was evident in the tissue sections. Dog No. 8 gave birth to a litter of pups on the 40th day after the second stage operation.

Microscopic examination of the artificial bile duct of dog No. 5 (Fig. 9) revealed that it had not retained its epidermal lining or its skin appendages except for one nest of sebaceous glands



In all three instances the tube had decreased in length and diameter, but at no point was its lumen smaller than 2 mm. (original diameter 7 mm.).

#### DISCUSSION

Skin implanted in the greater omentum fuses readily with its intra-abdominal bed. Such grafts heal along lines of junction between skin edges. When the graft is implanted in tubular form healing results in a tube with a continuous lining of skin. Rich vascularization of the dermis proves that the nutrition of the graft is well maintained by the omental circulation.

Healthy, living skin has sufficient resistance to survive in the presence of bile. It was noted in one instance (dog No. 1) that, although its epidermis was ulcerated at the time of the second stage operation, new epidermis had re-

generated to the point of a nearly complete lining within a period of 28 days.

Since bile leakage was not observed it appears that the two-layer suturing technique of anastomosis of the tube to hollow viscera is adequate. In order to minimize foreign body reactions and consequent fibrosis, absorbable suture material should be employed.

Split thickness are preferable to full thickness grafts because they are more likely to take. The grafts should be thin (e.g. 0.010 inch) so as to exclude the greatest possible amount of elastic tissue and other accessory skin structures. Buried hairs may stimulate a severe foreign body reaction.

Wound infection was a serious complication in three of our experiments. It delayed healing of free skin grafts in their beds and resulted in proliferation of constrictive fibrous tissue.

Examination of skin grafts in the omentum did not reveal gross changes in the microscopic appearance of the skin within periods as long as 34 days. No metaplasia was seen. At the second stage operation very little inflammation was observed in the skin-lined tubes of animals that had not experienced wound infections. The dermis and adjacent omental tissue was infiltrated by only a few foreign body giant cells and lymphoid cells. The zone of fibrous tissue between the dermis and omental tissues was very narrow and in places scarcely visible.

Wound infection was chiefly responsible for the partial biliary obstruction with jaundice which developed in dog No. 1 and dog No. 2 at 28 and 55 days, respectively. In both instances silk suture material was used in the anastomosis of the tube to the biliary tract and to the intestine.

Examination of the tubes of dogs Nos. 5, 6 and 8, which had conducted bile for 6 to 8 months, revealed uniform diminution in the diameters of their lumina. Additional constriction was apparent at the sites of their intestinal anastomoses. In these animals the inflammatory process in the walls of the biliary passages was the result of an ascending cholangitis in the absence of the protection normally afforded by the sphincter of Oddi. It is regrettable that none of these animals had a bile duct of sufficient calibre to permit replacement of a segment of the duct by a skin-lined tube in the presence of an intact sphincter.

Cirrhosis and cholangitis was most obvious in the animal (dog No. 5) in which a choledochoduodenostomy was made. In this case also the epidermal lining of the tube was almost completely replaced by biliary duct epithelium. In contrast, there was excellent preservation of the epidermal lining of the tubes in dogs Nos. 6 and 8, which were anastomosed to the jejunum. It seems probable that, had dogs Nos. 5, 6 and 8 been observed for much longer periods of time, at least partial biliary obstruction would have developed because of the presence of a mild, chronic inflammatory process in the walls of the biliary tree.

#### CONCLUSIONS

1. Free skin grafts survive when implanted in tubular form in the greater omentum of rabbits and dogs.
2. Tubular skin grafts in the omentum heal to form tubes with a continuous lining of skin and a mobile vascular pedicle.
3. Such tubes resist exposure to bile.
4. Regeneration of damaged epidermis may take place in the presence of bile.
5. Skin-lined tubes have been observed to function as biliary ducts for as long as 8 months without the development of biliary obstruction or stasis.
6. Mild to moderately severe hepatic cirrhosis and pericholangitis are likely to develop within 6 to 8 months in dogs whose biliary tracts are deprived of the sphincter of Oddi.

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Pericarditis is one of the most commonly overlooked clinical conditions. In recent years bacterial pericarditis, including the tuberculous type, has decreased, while pericarditis secondary to cardiovascular disease, uræmia, and malignancy has increased with the increase in the life span of the population.—G. R. Herrmann, *Am. Heart J.*, **61**: 43, 5, 1952.