ON THE SIGNIFICANCE OF THE ESCAPE OF STERILE BILE INTO THE PERITONEAL CAVITY

By Owen H. Wangensteen, M.D.

of Minneapolis, Minn.

from the department of surgery, university of minnesota

The ominous import of the discharge of infected bile into the peritoneal cavity following perforations in the inflamed extra-hepatic bile passages is generally conceded. McWilliams,[69] in reporting 108 operated cases of spontaneous perforation in the infected biliary system, states that the mortality was 48 per cent. In a study of peritonitis by Hirschel,[46] seven of the cases reported were due to perforations in the biliary tract. All died. J. F. Erdmann[29] has compiled thirty-four instances of spontaneous perforation of the gall-bladder during typhoid fever. Twenty-seven were not operated on. All died. Of the seven submitted to operation, four recovered. Noetzel[78] states that eleven cases of spontaneous perforation of the gall-bladder have come under his observation, six of which died. In an experimental investigation he established peritoneal-bile fistulæ in dogs and at the same time introduced bacteria into the peritoneal cavity. In almost every instance death quickly supervened due to a fulminant peritonitis. When bile alone was allowed to drain into the peritoneal space, or bacteria alone introduced, no untoward effect was observed. The malignant character of biliary peritonitis needs no emphasis.

The significance of the escape of sterile bile into the peritoneal space is not so generally agreed upon. Some of the early writers on this subject believed that the escape of bile into the peritoneal cavity was regularly followed by a fatal outcome. More recent observations would lead us to believe that the leakage of bile into the peritoneal cavity is attended with no great danger. Some state that sterile bile in the free peritoneal cavity is absolutely innocuous.

Larrey[60] wrote "Le epanchement des matieres bilieuses dans la cavite abdominale est mortel." John Bell[4] considered the escape of bile into the peritoneal cavity more dangerous than fæces or urine. Hennen said, "Nie ist Jemand meines Wissens von einer Verwundung der Gallenblase genesen." Duputryen[28] believed that wounds of the gall-bladder were regularly fatal from peritonitis. Chelius[15] stated that only with localization of the escaped bile, the establishment of an external fistula or removal of the bile by puncture was a favorable outcome possible. Guthrie[39] said "wounds of the gall-bladder are as far as is known, fatal."

In 1879, Thiersch[99] reported before the German Congress of Surgery the instance of a boy of twenty who died seven weeks following receipt of an injury to the biliary passages: three litres of bile had been aspirated. The only other instance of death following rupture of the biliary passages that had come to his attention was the case of Drysdale,[21] where death occurred fifty-three days after rupture of the common bile duct. It was his opinion that the escape of sterile bile into the peritoneal cavity was attended with no great danger. Lesser,[60] in discussing the case of Thiersch, reported on some experimental work done by Bostroem which would indicate that large amounts of bile in the peritoneal cavity are innocuous. In 1892, in an editorial article in the

ANNALS OF SURGERY, Samuel Lloyd[97] stated that no deleterious effects result from the escape of bile into the peritoneal cavity. In the same journal is abstracted a case report of Hermes[43] from the *Deutsche Medizinische Wochenschrift* in which a successful outcome is reported following operation for the escape of bile into the peritoneal cavity after trauma to the biliary tract. The editor appends the following note: "This is an admirable illustration of the comparative harmlessness of the escape of bile into the abdominal cavity and corroborates the instances reported in the editorial in the August ANNALS."

Before the Philadelphia Surgical Society in 1904, J. H. Jopson[50] and W. J. Taylor[97] reported cases of spontaneous rupture of the gall-bladder associated with unusual toxic symptoms. In both these instances, however, calculi were present and the bile presumably infected.* Both patients recovered. LeConte, at the same time, in reporting another instance and discussing the cases of Jopson and Taylor, stated "that so many cases had been reported where bile was present in the peritoneal cavity without producing profound toxic symptoms that one must eliminate many other factors before concluding that such toxæmia is caused by the peritoneal absorption of bile." In the same discussion, W. J. Hearn† gave it as his opinion that bile in the peritoneal cavity produces no more toxic effects than does any other foreign body. J. H. Gibbon[36] states that cases had come to his attention "where bile had been present in the peritoneal cavity for many months without producing untoward effects." He would rather believe with LeConte[61] that bacteria were responsible for the symptoms that developed from leakage in the biliary tract.

Cohnheim,[16] Edler,[24] Laehr,[58] and Hahn[40] believe that sterile bile in the peritoneal cavity provokes a chemical peritonitis and ascribe the untoward results occasionally observed after bile leakage to injury to the peritoneum.

Schlatter[89] says that its presence in the peritoneal cavity is well tolerated and that bile possesses absolutely no danger for the peritoneum. The danger of bile leakage he believes lies not in peritonitis, but in a toxic influence due to overloading the body with the biliary constituents.

Guibe[35] states that biliary peritonitis is a misnomer and would rather designate the accumulation of sterile bile in the peritoneal cavity as choleperitoneum. Such a condition of itself this author maintains is well tolerated and does not bring about death. The real danger in the escape of bile into the peritoneal cavity Guibe says is infection. Dormont,[20] too, states that any ill effects observed following bile leakage is due to infection. Noetzel,[73] McWilliams,[69] Orth,[79] Sick and Fraenkel,[91] Buchanan,[13] Ritter[84] and Burckhardt[14] state that large amounts of sterile bile in the peritoneal cavity are well tolerated.

Courvoisier[17] collected 34 instances of subcutaneous rupture of the biliary passages following trauma, of which 22 died and 12 recovered. In no instance did a patient recover without puncture or operation. Courvoisier stated that animal experiments demonstrate the harmlessness of the presence of sterile bile in the peritoneal cavity, but despite the uniform mortality in the untreated group of biliary leakage concluded that clinical experience also substantiated the idea and that bile in the peritoneal cavity when sterile was relatively harmless. That a toxic action of bile obtained through absorption be considered as being doubtful. Terrier and Auvray,[86] in a review of injury to the

* The investigations of Naunyn,[76] Leubuscher,[64] Gilbert and Girode,[37] Mieczkowski[72] and Mikaye[75] demonstrate that the bile of healthy animals is sterile. The contention of Fraenkel and Krause,[21] and Ehret and Stolz[25] that bacteria are present in normal bile is probably not correct. Duclaux,[22] Netter and Martha[77] and Mikaye[75] have shown that the bile in the terminal portion of the common duct regularly contains bacteria. The examination of the bile from gall-bladders that contain calculi by a number of investigators shows that bacteria are regularly present,[74, 80] even though their demonstration may be difficult. Their virulence on animal innoculation is often minimal.

† Discussion of papers by Jopson, Taylor and LeConte.

bile passages following trauma accept the conclusion of experimental investigators that sterile bile in the peritoneal space of animals is attended with no danger, but reiterate the statement of Courvoisier that no case of rupture of the biliary passages has been cured without puncture or incision.

Lewerenz [65] reported a successful outcome after rupture of the common bile duct in a boy of two and one-half years, and collected 63 other instances of injury to the gall-bladder and bile ducts from the literature. The absorption of the bile from the peritoneal cavity in these instances he considered the usual cause of death, the bile salts being responsible for the lethal outcome. Stierlin [96] also states that the resorption of bile in these instances gives rise to a fatal toxæmia when the bile flows into the peritoneal cavity for a long time. The loss of bile from the intestine he believes hastens death. Ricketts [83] combined in a report 273 instances of spontaneous perforations and traumatic ruptures of the gall-bladder and noted the better prognosis in the traumatic group. Amante [1] collected 101 instances of subcutaneous rupture of the biliary passages and states that without intervention such an injury is usually fatal, due to the toxæmia resulting from the absorbed bile. Thöle [100] in a monograph on the subject, says that spontaneous rupture of the inflamed biliary tract is much more serious than traumatic rupture of the normal bile passages. Death is due to cholæmia, loss of bile from the intestinal tract and inanition in the latter group. Kehr [51] once of the opinion, that sterile bile was without effect in the peritoneal cavity, now states [52] that continued leakage of bile into the peritoneal cavity is a serious occurrence due to the general intoxication consequent upon the absorbed bile salts. Guibe, Ritter, and more recently Burckhardt, have insisted that death from cholæmia following rupture of the bile passage has never been observed.

A number of experimental investigators have concerned themselves with this problem, and with one exception have all concluded that sterile bile may be present in the peritoneal cavity without harm. Ehrhardt [36] ligated the supraduodenal portion of the common bile duct in twelve dogs and cats, cut the duct above the ligature and slit the proximal end a little. His animals died within two to six days with a progressive icterus. At necropsy there was only a little bile in the peritoneal cavity. The peritoneal surfaces were bile stained, but were otherwise smooth and glistening. The bile was sterile. Death he attributed not to a chemical peritonitis, but to cholæmia from the absorbed bile. In two cats he cut a hole in the gall-bladder and placed a culture of dead B. coli in the peritoneal cavity. Neither of these animals died of infection or cholæmia at the end of fourteen days. Two experiments done subsequently [37] with staphylococci gave the same results. Ehrhardt concluded that bile depressed the virulence ‡ of bacteria and that infection protected against death from cholæmia.

Noetzel [78] cut a hole in the gall-bladders of seventeen rabbits. Sixteen recovered without effect. Only one died. Noetzel concluded that large cuts in the gall-bladder heal readily § and that the escape of bile into the peritoneal cavity is innocuous.

Bostroem, according to Lesser,[63] was also unable to observe any injurious effect from the leakage of bile into the peritoneal cavity of animals, and concluded that large amounts of sterile bile are well tolerated by the peritoneum and that fistulous openings in the gall-bladder close quickly.

Fraenkel and Krause [41] injected bile into the peritoneal cavity of guinea-pigs and dogs without observing any untoward effects. After cutting the gall-bladder with scissors in dogs the result was the same. When the dogs were killed two to five weeks later, the wounds in the gall-bladders had healed or were sealed with omentum or loops

‡ The delayed death in this group of animals in all likelihood was due to a localization of the process by omentum or loops of intestine. When infected bile escapes into the peritoneal cavity, the process is usually well-walled off. Sterile bile on the contrary usually escapes into the free peritoneal space.

§ Enderlen and Justi [38] have studied the repair in wounds of the gall-bladder microscopically and find that healing occurs quickly.

of intestine. It was their conclusion that the escape of bile into the peritoneal space was without danger. Kehr,[62] and Terrier and Auvray[96] state that Emmert, Hering, and Villaderbo, Campaignac, Ammussat and Schwartz have made similar experiments and have concluded that the presence of sterile bile in the peritoneal cavity is without significance.

The writer believing that in the experimental animal the establishment of well-functioning fistulæ is essential to determine the significance of the escape of sterile bile in the peritoneal cavity, ligated the supraduodenal portion of the common bile duct in six dogs and cut a hole in the gall-bladder at the same time. All of these animals died within twenty-four hours. At necropsy the bile in the peritoneal cavity was sterile. In two rabbits this same procedure was done. Both died within twenty-four hours.

In four other dogs the common bile duct was divided, in two the distal end was tied, in the other two it was left open. All these animals died within forty-eight hours. In two rabbits the common bile duct was divided and the distal end left open. Death occurred within forty-eight hours.

When well-functioning biliary fistulæ are established in animals, death regularly obtains due to the toxic action of the absorbed bile. In a few instances, the peritoneal surfaces were somewhat reddened, presenting the appearance of underdone beef. This appearance of the peritoneum in traumatic rupture of the biliary passages has also been noted.[101] Cultures of the bile from the peritoneal cavities of these animals were uniformly negative for bacteria. The irritating action of the bile salts was in all likelihood responsible for this occasional reddened aspect of the peritoneal surfaces.

Of the solid constituents of bile, cholesterol and mucin can be by fairly general consent ruled out of consideration as not being responsible for the toxic symptoms that develop following the peritoneal escape of bile. Some of the early writers believed that the bile pigments were the toxic element in bile. Notably among these were Frerichs,[32] Bouchard,[9] de Bruin[11] and Plaesterer.[81] A more recent experimental study by King and Stewart[58] would also tend to bear out the idea that the bile pigments were toxic. These authors state that the amount of bile salts in a toxic dose of bile given intravenously is insufficient to bring out the symptoms observed. Meltzer and Salant[72] have attributed this same toxic action of bile to the bile salts. Bunting and Brown[13] ascertained that small amounts of bile injected into the peritoneal cavity of rabbits and rats were fatal. They ascribed the fatal issue to a toxic effect on the myocardium but made no attempt to determine whether the salts or the pigment was the lethal factor.

Among the early writers on this subject, Röhrig,[85] Feltz and Ritter,[30] Leyden[66] and Rywosch[87] believed that the bile salts were responsible for the toxic action of bile. Exhaustive investigations by Stadelmann[94, 95] and Bickel[6] lend tenable support to the idea that bile salts are the toxic element in bile.

Biedl and Kraus,[7] in reviewing the toxic effects of bile, state that bile salts are strongly hæmolytic for blood. In sufficient concentration they cause a coagulation of myosin, such that muscle loses its contractibility. When

applied to a motor nerve, convulsive movements of the innervated muscles may be elicited. If introduced intravenously a slowing of the pulse with a fall in arterial blood pressure occurs. After toxic intravenous doses, a comatose state, convulsive seizures and death are the usual sequelæ.

In the experimental animal when all the bile escapes into the peritoneal cavity death ensues quickly within twenty-four to forty-eight hours. When reference, however, is made to reports of cases observed clinically in which the common duct was ruptured and a condition present analogous to that in the experimental animal just mentioned, a very different sort of situation is seen to obtain. Meissner [71] collected 12 cases of injury of the common bile duct. Eight, or 75 per cent., of these died, but in only one instance did death occur within twenty-four hours from the receipt of the trauma. Two died thirty-three days [92, 96] after the injury and a third case [21] fifty-three days later, when at necropsy the common duct was found completely divided.

Meissner mentions 7 other ruptures of hepatic ducts, in 4 of whom the outcome was lethal. These died from one to eight weeks after the injury.

Courvoisier,[17] in commenting on the cause of death following subcutaneous wounds of the biliary tract, stated that in the 34 cases collected by him only 5 died within twenty-four hours. In 3 of these, autopsy demonstrated bleeding from the liver. A sixth case died after forty-eight hours.

Landerer [60] aspirated a total of 35 litres of bile from the peritoneal cavity of a boy of sixteen at successive punctures with a successful outcome. Petersen [80] records the instance of a boy from whose peritoneal cavity 5600 c.c. of bile was aspirated and two rents in the gall-bladder successfully repaired five weeks after a wagon had passed over the boy's abdomen. Garrett [35] removed a total of 16 quarts of bile by aspiration from the peritoneal cavity of a man who fell across a beam. Twenty days after the injury, a tear in the posterior wall of the common duct was found at operation. Drainage was established and the patient recovered. Uhde [100] removed 14½ kilograms of bile by abdominal paracentesis twenty-three days following an injury in a man of twenty-nine. Thirty-seven days later 9¼ kilograms were again removed and the patient recovered. J. F. Thompson [101] records the instance of a man thrown from a cart from whose peritoneal cavity 4 quarts of bile were aspirated at one time. Later 5 quarts and "seven or eight times several quarts of bile were removed" with a favorable outcome following operation.

Kulenkampff,[55] Waugh,[104] Kehr,[51] Willard,[106] Barling,[3] Garre,[34] Dirk,[29] Hildebrandt,[46] Fryer,[33] Barlow,[3] and others, have reported instances where bile was present in the peritoneal cavity for a long time following rupture of some portion of the biliary tract. Large quantities of bile were evacuated at operation or removed by puncture often at a date remote from the time of injury and the patients recovered.

In some of these instances it is not to be doubted that a dilution of the bile probably occurred through the irritation of the peritoneum and a consequent serous exudation. However, these instances substantiate beyond doubt the fact that oftentimes large quantities of bile may remain in the peritoneal cavity over a considerable portion of time, the patient meanwhile continuing in a fairly good state of health.

It has been suggested that the only deleterious effect from the escape of bile into the peritoneal cavity is occasioned through the loss of bile from the intestinal tract.[21, 59, 92, 90] The exhaustion and inanition that these patients present would give credence to this belief, but when it is remembered that complete external biliary fistulæ have been present in patients over a number of years without untoward effects, the loss of bile from the intestinal tract

alone can scarcely be assigned as the responsible factor for the lethal outcome when the bile escapes into the peritoneal cavity. Courvoisier [17] mentions instances in which complete external biliary fistulæ were present 2, 3, 5, 6, 8 and even 12 years without undue ill consequence upon the patient's well-being. Dogs in which complete external biliary fistulæ are established, it is true, frequently die [49, 96] of inanition and in patients, too, apathy and anorexia occasionally are observed when all the bile is discharged to the outside. The administration of bile salts in the form of ox bile usually remedies the condition. The occurrence of osteoporosis [90] in the bones of the experimental animal and in patients who have had complete external biliary fistulæ over any length of time has been noted.

Schiff [88] early observed that when complete external biliary fistulæ were established in dogs that the solid content of the excreted bile diminished markedly. The decrease in the bile salt content was similarly marked. When ox bile was fed to these animals the excretion of the bile salts increased. Stadelmann's researches [94, 95] also corroborate these findings of Schiff. Stadelmann states that when bile salts are fed that they are excreted in the bile to two-thirds of the ingested amount within ten to twelve hours. Wisner and Whipple [106] have noted the fluctuation in bile salts in fistula bile with increase or decrease of food.

When bile is excluded from the intestine and lost from the body through a fistula, therefore, the amount of bile salts is markedly diminished. May the same condition obtain in exclusion of bile from the intestine alone, such that patients with total occlusion of the common bile duct frequently escape an early death from the toxic bile salts and may the same cause account for the delayed death in cases where bile escapes into the peritoneal cavity.

The normal daily output of bile salts according to Weintraud [105] and Biedl and Kraus [7] is about 8 to 11 grams. If this production continued in obstructive jaundice or in biliary leakage, certainly the patient should succumb at an early date to the toxic action of the bile salts. Macleod [68] says that gall-bladder bile contains about 10 to 20 per cent. solids, whereas in fistula bile only 3 per cent. is present. Brand,[10] in reviewing all the published cases that had come to his attention up to 1902 where bile had been subjected to quantitative examinations, stated that the solid content of bile in fistula cases was 1 to 4 per cent., for gall-bladder bile 20 per cent. The concentrating activity of the gall-bladder is of course partially responsible for the greater solid content of gall-bladder bile. The factor of loss of bile from the intestine to the outside, however, is undoubtedly the more significant.

Bischoff [8] could find only .34 gram of bile salts in the urine in marked icterus. He didn't believe that bile salts were formed in less amount in jaundice, but thought that they disappeared in the blood. Kühne [54] was unable to find bile salts in normal urine. But Stadelmann [94] says that Dragendorff and Hönne were able to recover the crystals of bile salts in normal urine. Intravenous injections of bile salts by Huppert,[49] Leyden [59] and Hoppe-Seyler ¶ demonstrate that a very minor portion of these salts are excreted in the urine. Stadelmann [94] states that bile salts have not been found in blood, even though Friedlander claims to have found .0075 grams of sodium glycocholate in 100

grams of blood. Frerichs[88] could find no trace of bile salts in the blood or urine of jaundiced patients after several attempts. Thirty litres of urine were used by Hoppe-Seyler[65] to get a qualitative test for bile salts in the urine of a jaundiced patient.

Professor Hilding Berglund[5] informs me that there are no reliable quantitative methods for determining bile salts in blood and urine. We must, therefore, turn to instances in which bile salt determinations have been made on bile following prolonged occlusion of the common bile duct, in which external drainage has been established. Unfortunately such determinations are rare and subject to the criticism that the bile salt determinations were made on fistula bile, which normally is poorer in all the solid constituents of bile that is ordinary bile.

Yeo and Herroun[108] report quantitative examinations on bile of a man who had been jaundiced six months. Of the total daily output of bile only 1.28 per cent. to 1.416 per cent. were solids. Of this amount .165 per cent. was sodium glycocholate and .055 per cent. sodium taurocholate. Hammarsten[41] reports examinations on 7 cases operated by Lennander, in which cholecystostomy had been done. Two of these patients had been jaundiced, one about three weeks, the other six weeks. The bile salt content in all 7 cases was low. In the 2 patients who had been jaundiced no remarkable decrease over the fistula bile in the other 5 instances was noted.

In only one instance to the writer's knowledge have quantitative bile salt determinations been done on the escaped bile following subcutaneous ruptures of the biliary tract. Eight days following such an injury in a man of twenty-four, Kulenkampff[68] aspirated 9.6 litres of bile, again ten days later ¾ of a litre, and eighteen days afterward 1½ litres more. Hausmann made quantitative studies on the removed bile for bile salts. The first specimen contained 401 milligrams of bile salts per 200 c.c. A determination on the second specimen showed only 18 milligrams present in the same amount.

In external biliary fistula the amount of bile salts excreted in the bile diminishes markedly. In obstructive jaundice and leakage of the bile in the peritoneal cavity, where the bile salts are excluded from the intestine the same condition apparently obtains.

Stadelmann[94] postulates a circulation of the bile salts in the organism. They are excreted through the liver, absorbed from the intestine largely *via* the thoracic duct, he believes, and then reëxcreted through the liver. Such an explanation would be inadequate to account for their seeming diminution in the escape of bile into the peritoneal cavity. The absorption from the peritoneal cavity, save in those rare instances where bile is encysted (cases of Drysdale,[21] Thiersch,[99] Ratjen[82] and Labrosse[56] would probably be unusually rapid.|| If Stadelmann had contended that the circulation of the salts was completed through the portal vein instead of the thoracic duct, it would be reasonable to assume that any exclusion of bile from the intestine would be associated with a diminution in the bile salt production. Schiff's[88] observation that injection of bile salt into a mesenteric vein also increased the excretion of bile through an external fistula would be in consonance with such a contention.

In obstructive jaundice, in addition, the liver cells may be damaged[105] so that the bile salt production does not continue even though the material necessary for its synthesis may not be wanting.

¶ Quoted by Stadelmann.[94]

|| Sterile bile is rarely encysted, though this would appear to be the rule with infected bile. Following the escape of bile into the peritoneal cavity more than half the cases are jaundiced.

The reason for the more rapid death in the experimental animal when well functioning bile fistulæ are established probably lies partially in the explanation that human bile contains largely glycocholic acid and relatively little taurocholic acid. Brand [10] found that this relationship of glycocholic to taurocholic acid in man was 1 : 4.5 to 1 : 5.4. In reports of other examinations collected by Brand, this disproportion was often as great as 1 : 7.3 to 8. Dog bile, on the contrary, is largely taurocholic acid. A number of investigators even deny that dog bile contains glycocholic acid. Inasmuch as the taurocholic bile salts are twelve to twenty times more toxic than the glycocholic, the quicker death in the dog should be anticipated.

As concerns the treatment of instances in which bile escapes into the peritoneal cavity following injury of the bile passages, the early removal of the bile, repair of the fistulous opening and drainage are indicated. In rupture of the gall-bladder, cholecystectomy is the operation of choice; in injury to the ducts repair of the defect. When one of the major ducts has been completely severed a complete circular suture is to be avoided because of the subsequent danger of stricture formation.[100] A circular suture of three-quarters of the circumference of the duct with drainage through a Kehr T catheter is the method of choice in repairing the defect. Instances have been reported where the common duct was completely severed, suture impossible and the patient recovered following tamponade alone.[71, 86] Ligation of a severed hepatic duct, though a safe procedure in animals would seem hazardous to apply to man. After complete severance of the common duct, ligation of the proximal end followed by cholecystenterostomy has been done.[65]

In most of the instances reported in the literature where large quantities of bile have escaped into the peritoneal cavity, the patient has shown marked evidence of shock, such that immediate interference would be out of the question. It is interesting, however, that death from shock is rare. Where a diagnosis of the escape of bile into the peritoneal cavity can be reasonably entertained following a severe injury to the abdomen, in which a movable effusion can be demonstrated and signs of peritoneal irritation are present, and the patient's condition such that surgical interference is deemed unwise, operation may be deferred, a diagnostic puncture done, and if bile is recovered, as large a quantity as possible removed through the aspirating needle. Numerous instances of recovery following aspiration alone have been recorded, but the virtue of such a procedure lies in this: that the patient is not subjected to a major procedure while the patient is in a dangerous plight. Through removal of the bile, repeated if necessary, his condition may be so improved that operation may be done later with but little risk.

SUMMARY

The leakage of sterile bile into the peritoneal cavity is not innocuous. The experimental animal dies of cholæmia due to the toxic action of the bile salts within a short time when well functioning biliary fistulæ from which bile escapes into the peritoneal cavity are established. The escape of any

considerable amount of sterile bile into the peritoneal cavity of man following subcutaneous rupture of the normal bile passages, unless removed, is always fatal. No instance of recovery in such an event has been recorded without removal of the bile by operation or puncture. The cause of death is cholæmia. The loss of bile from the intestinal tract is a contributing factor, but at the same time probably also accounts for the delayed death in untreated cases, through a diminution of bile salt production when bile fails to reach the intestine. The more rapid death in the dog following the extravasation of bile lies partially in the explanation that dog bile is largely the more toxic taurocholic acid, whereas, human bile contains relatively more of the less toxic glycocholic acid.

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