A fully automatic organ pressure sensitive apparatus for dislodging and removing obstructions in body cavities or organs by both delivering (17) and removing (20) fluid thereto, operable by high rate continuous or intermittent infusion of fluid solvent over a set pressure range to effect rapid dissolution and removal of the obstruction without complications to the patient. By continuous feedback monitoring (22) of fluid pressure in the bodily organ or cavity (19) of interest, the apparatus can constantly vary infusion and aspiration rates to maintain the set pressure range. If the pressure persists above or below the set range, the apparatus activates a safety feature (32) leading to a period of maximal aspiration and cessation of infusion, followed by cessation of solvent transfer and triggering of an alarm (34) to alert the operator.
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"APPARATUS, CATHETER AND METHOD FOR CHEMICAL CONTACT
DISSOLUTION OF GALLSTONES"

This application is a continuation-in-part of copending
application Serial No. 07/180,099 filed April 11, 1988 which
was a continuation-in-part of application Serial No.
06/871,775, filed June 9, 1986.

BACKGROUND OF THE INVENTION

For most individuals who suffer from gallstones, the
treatment of choice is to have a cholecystectomy, or surgical
removal of the gallbladder. Each year 500,000 such operations
are done in the United States alone. Recently, because of the
cost, prolonged recuperation time and possible side effects
associated with this surgery, methods have been developed for
chemically removing gallstones in situ. Generally, this
procedure involves inserting a catheter into the gallbladder
followed by infusing a chemical solvent capable of dissolving
the gallstone. The procedure thus avoids the need for and
attendant risk of surgery.

A variety of chemical solvents have been tried and found
to exhibit varying efficiencies of gallstone dissolution,
depending on the chemical nature of the gallstone. Gallstones
are generally composed of cholesterol or calcium salts,
particularly calcium bilirubinate and calcium carbonate.
Lipid solvents are effective at dissolving cholesterol
gallstones, whereas these solvents have little or no
solubilizing effect on gallstones composed of calcium salts.
Thus, diethyl ether readily dissolves cholesterol gallstones,
and other solvents such as mono-octanoin, and octadiol
(glycerol-1-octyl ether) also have good solubilizing
properties. Unfortunately, few if any solvents are
satisfactory for dissolving calcium gallstones. The invention
herein will therefore find principal utility in cholesterol
gallstone removal. It has been recognized that ether
compounds such as diethylether have excellent cholesterol
solubilizing properties, low viscosity and very good kinetic
solubility but diethylether is hazardous since it boils below
body temperature. Recently methyl tert-butyl ether (MTBE),
a solvent hithertofore used primarily as a gasoline additive
and a chromatographic solvent media, has been used for
gallstone dissolution since it exhibits all the properties of
ethers. Moreover, MTBE boils above body temperature and the
solvent rapidly dissolves the gallstones without damaging the
mucosa of the gallbladder.

The effectiveness of such new solvents has led to
considerable activity focused on developing apparatus and
methods for delivering MTBE and similar solvents to patients
suffering from gallstones in ways to most rapidly and
effectively solubilize gallstones without the complications
arising from introducing such solvents into the body. (For
brevity herein, the description will be with respect to use
of the MTBE as a solvent. It will be recognized, however,
that this invention will be applicable to a number of
different solvents).

Physicians currently treat cholesterol gallstones by
infusing MTBE into the gallbladder through a percutaneously
positioned catheter through which MTBE is manually passed
using glass syringes [Walker, Lancet, 1, 874 (1891);
Shortsleeve, Radiology, 153, 547 (1984); and Teplick,
Radiology, 153, 379 (1984)]. Additionally, physicians have
available fixed volume syringe pumps, such as described in
U.S. Patent No. 4,655,744 to Thistle et al. to infuse and
aspirate MTBE. There are several complications associated
with either the manual infusion or the fixed volume pump-
assisted infusion procedure.

When MTBE is delivered manually via glass syringes or
with the aid of a fixed volume-cycle pump, spontaneous
gallbladder contraction or over filling of the gallbladder
cannot be detected or controlled. Consequently, MTBE
periodically empties into the duodenum, producing duodenal
mucosal injury, which in turn produces nausea, vomiting,
duodenal erosions and accompanying pain of sufficient
intensity to necessitate frequent administration of
analgesics. In addition, when in the duodenum, MTBE can be
absorbed into the blood stream, which in turn may result in
somnolence or hemolysis and concomitantly the presence of the
intense and irritating MTBE odor in the patient's breath.

Other problems associated with the manual or pump-
associated syringe method involve inefficient removal of
insoluble gallstone particles which constitute varying
percentages of cholesterol gallstones. Such particles are
often left behind in the gallbladder, after MTBE dissolves the
cholesterol portion, in procedures involving syringes or
syringe pumps. These particles often serve as the nidus for
new gallstone formation. Additionally, both procedures are
time consuming, laborious and require individuals that are
highly skilled in their use. Consequently, the procedures are
expensive because of the attendant costs associated with
having a highly skilled staff of professional people to
perform the procedure for prolonged times, often 12 hours or
more. In addition, a fixed volume syringe pump can not
prevent bile from entering the gallbladder during the course
of its secretion by the liver. Bile in the gallbladder
impedes the solvent's contact with stones and hence delays the
process of dissolution.

It is obvious that delivering MTBE to a patient requires
the utmost care to avoid releasing the solvent into the
patient's bodily fluids or outside the area of treatment.
Thus a key consideration in developing devices used in the
chemical therapy of gallstone dissolution is ensuring the
controlled delivery and removal of the solvent used to
dissolve the gallstones. Considering that studies have shown
that solvents such as MTBE are injurious if they pass into the
intestine where they get absorbed, there is a critical need
for devices that ensure that such chemicals will not be
released during chemical therapy for gallstone removal. At
the same time such devices must be able to maintain high
solvent circulation rates into the gallbladder to create the
necessary turbulence that will enhance dissolution and aid in
 evacuating the insoluble residue.

Also, because of the need to ensure containment of
solvents, in addition to the safety features described above,
a suitable device should be "user friendly" and not require
the presence of highly skilled technicians to run the device.
Further, for the same reasons, it should be easily
maintainable.

With a little reflection, it becomes apparent that there
are considerable hurdles to surmount if one is to develop a
device that has the features described above. For instance,
it must be "intelligent" and capable of sensing instantaneous
changes in gallbladder pressure brought about by gallbladder
contractions or by infusing the solvent, and rapidly relay
this information to controlling feedback circuits. This is
a crucial feature for such a device. If a gallstone should
in some way prevent the necessary circulation of the solvent
through the gallbladder, a critical pressure will build up,
possibly rupturing the organ or causing leakage of the solvent
from the gallbladder through the cystic duct into the common
duct and intestine. Thus the device must be "intelligent" in
the sense that it senses gallbladder pressure changes over a
predefined range and reacts fast enough to keep the pressure
in that range, shutting down or reacting appropriately if the
pressure persists outside the range. Moreover, it would be
desirable to have a device that not only is capable of
shutting down, but actually can flush out any debris causing
the blockage, and resume normal operation should the debris
be removed. Such device should prevent intra-gallbladder
pressure from rising above leakage limit and from falling
below the pressure under which bile will be sucked into the
gallbladder from the biliary duct.

SUMMARY OF THE INVENTION

The invention herein comprises an apparatus and a method
for its use which are for therapeutic treatment of obstruc-
tions in bodily organs by high rate solvent circulation,
particularly for gallbladder or common bile duct stones. The
apparatus has the desirable feature of continuous high rate
infusion and aspiration while preventing solvent leakage from
the bodily organ being treated. The apparatus comprises a
forward or reverse acting solvent delivery means that is
linked via a pressure transducer to a feedback controller
circuit.

The apparatus is preset to perfuse within a set pressure
range. Continuous feedback of true intraluminal organ
pressure to a controller circuit via the transducer controls
the rate and the net direction of solvent delivery by the
apparatus and is determinative of whether the apparatus acts
in the forward or reverse mode. Over this range the solvent
is constantly passed from a reservoir into the gallbladder,
and from the gallbladder it is aspirated to a suitable
receptacle. Delivery and removal of the solvent is at a rate
sufficient to effect gallstone dissolution and fragmentation,
agitation and aspiration of insoluble fragments. Should there
be an increase in pressure, a feedback loop switches the
device into a high pressure mode, thereby diverting the
solvent away from the gallbladder. If after a predetermined period of time the pressure sensing transducer readings from the gallbladder indicate a return to normal operating pressure range, the device automatically reinitiates the normal infusion and aspiration (perfusion) mode.

An additional feature of the invention is a self purging mechanism. After a preset interval, if the pressure does not decrease, the device enters a reverse mode to purge the aspiration port of the catheter, whereby fluid is aspirated backward through the infusion port and infused through the aspiration port to purge for discrete short intervals, during which time the pressure in the organ is continuously monitored. Once the blockage is removed by this "self-purging" action, the pressure transducer again indicates normal operating pressure, and the device resumes action in the normal pressure mode. However, should the obstruction not be removable after a predetermined number of purge cycles, an alarm circuit is activated, so notifying the user. A further feature of the invention is that it is able to distinguish clinically significant pressure changes occurring within the gallbladder which leads to emptying of gallbladder contents into the duodenum from those clinically insignificant changes arising as a result of coughing, laughing or like behavior. This feature prevents needless changes or operating modes.

A further aspect of the invention is a catheter for the contact dissolution of gallstones having a solvent infusion lumen and a solvent aspiration lumen in side-by-side relationship. The catheter is sized for introduction of its distal portion into the gallbladder from outside the body. Each lumen has at least one opening in the distal portion for communication between the gallbladder and a remotely located pump. A third lumen provides a means to continuously sense intra-gallbladder fluid pressure and to transmit an indication
thereof to the controller, for control of infusion and
aspiration of solvents via the lumens. An aspect of the
invention is that the cross-sectional area of the aspiration
lumen is larger than the cross-sectional area of the infusion
lumen. Fluid moves into and out of each lumen by a series of
openings in the walls of the catheter. The cross-sectional
area of each opening is less than the cross-sectional area of
the lumen with which the opening is in communication. The
catheter further includes a retention means to prevent the
catheter from being dislodged from the gallbladder. The
retention means is a curved formation of the distal portion
of the catheter. The pressure sensing means is located to lie
at the inner radius of the curved formation to prevent its
blockage by the mucosa of the gallbladder. Alternatively, the
retention means may be an inflatable balloon located adjacent
to the distal portion.

A tension string for holding the distal portion of the
catheter in a curved configuration is included. The catheter
also has a string passage lumen in which the string is
located. Alternatively, the string may be located in either
the aspiration lumen, the infusion lumen or the pressure
sensing lumen.

The opening at the distal end of the catheter is in
communication with the aspiration lumen. The catheter has at
least one aspiration opening, in the wall of the catheter in
communication with the aspiration lumen, which is located
proximal to all infusion openings. The proximally-located
aspiration opening is located adjacent to the point of entry
of the catheter into the gallbladder when the catheter is in
position for operation.

The lumen and aspiration opening at the distal end of the
lumen are constructed and arranged to enable the catheter to
pass over a guide wire. The catheter is made of material, for
example polyurethane, which is resistant to the solvent to be infused into said gallbladder.

The means for sensing the pressure of fluid within the gallbladder includes a third fluid pressure transmitting lumen extending side by side with the infusion and aspiration lumens and having a distal opening in the distal portion of the catheter. The lumen is constructed to communicate intra-gallbladder pressure to a remotely located pressure transducer via a hydrostatic fluid column. The means for sensing the pressure of fluid within the third lumen comprises a pressure transducer located at the proximal portion of the catheter. Alternatively, the pressure transducer may be located at the distal end of the catheter and provide in situ gallbladder pressure measurements. Such transducers for in situ use can be piezoelectric, or fiberoptic, and may be removably inserted in a lumen of the catheter. The wires or fiber of an in situ transducer located at the distal end of the catheter can pass through the pressure lumen, infusion lumen, or aspiration lumen or may be embedded into the catheter's wall. The catheter has a structural formation at its proximal end that permits it to be used only with a solvent delivery system having a predetermined mating structural formation that prevents inadvertent use with non-mating systems. Alternatively the catheter has an electrical or fiberoptic connection at its proximal end that permits it to be used only with a solvent delivery system having a predetermined electrical or fiberoptic connection.

One aspect of the invention is a microprocessor programmed to execute an algorithm in response to an input pressure signal derived from the gallbladder through a pressure determining module; a pump control module, to control the speed and direction of an infusion pump pumping solvent through an infusion lumen into the gallbladder of the patient.
and an aspiration pump pumping solvent through an aspiration lumen out of the gallbladder of the patient; and a response determination module to control the functions of the pump control module in response to the pressure determinations of the pressure determining module. The response determination module generates an alarm and initiates maximal continuous aspiration by both infusion and aspiration pumps in response to a number of intra-gallbladder pressure conditions including: no pressure variations of a predetermined amplitude detected for a predetermined period of time; abnormal pressure detected for a predetermined period of time or after predetermined volume has been used to purge said aspiration lumen; more than a predetermined number of purge cycles occurring within a predetermined period of time; detected pressure remaining less than a lower set limit for a predetermined period of time or the system being unable to maintain the pressure within normal range for a predetermined period of time.

The response determination module also stops infusion and maintains aspiration in response to intra-gallbladder pressure exceeding an upper set limit and aspirates through the infusion lumen until the pressure falls to an acceptable range. The response determination module then reverses flow to purge the aspiration lumen. The module also stops aspiration in response to the condition wherein the pressure is less than the lower set limit.

Another aspect of the invention is a means for continuously measuring the pressure within the gallbladder of a patient and a means for controlling the infusion and aspiration of a solvent into the gallbladder in response to those measurements to maintain said pressure within the set limits.

A further feature of the invention is a method for
dissolution of gallstones comprising the steps of continuously measuring the pressure within the gallbladder of a patient and controlling the infusion and aspiration of a solvent into the gallbladder in response to those measurements. The method further comprises the step of periodically measuring the amount of cholesterol in the solvent and replacing the solvent when the cholesterol concentration in the solvent reaches a predetermined concentration limit.

The method further comprises, prior to introduction of solvent into the gallbladder, the measuring of a critical leakage pressure at which fluid in the gallbladder discharges into an adjacent part of the body, and using the value of that pressure for controlling the infusion and aspiration. The step of measuring the critical leakage pressure comprises the injection into the gallbladder of a radiopaque dye at increasing pressure until the discharge of the dye is observed radiographically. The amount of pressure required to cause the leakage of dye is recorded as the critical leakage pressure and the amount of fluid required to fill the gallbladder is the available volume. The step of infusing the solvent into the gallbladder occurs at a rate sufficient to create solvent turbulence adjacent the gallstones.

An aspect of the invention further includes a system, including a system bus; a microprocessor in communication with the system bus; a memory for holding algorithms, the memory in communication with the system bus; an analog to digital converter having an input terminal for receiving an analog signal representative of the intra-gallbladder pressure and an output terminal for applying digital signals representing the pressure on said system bus; a pressure transducer having a pressure sensor and an output terminal, the output terminal of the pressure transducer in communication with the input terminal of the analog to digital converter. The pressure
transducer generates a pressure signal related to the pressure
of the solvent within the gallbladder.

The system also includes a reservoir, for filling with
a gallstone dissolving solvent, an infusion pump connected by
conduits to pump solvent from the reservoir into the
gallbladder, and an aspiration pump connected by conduits to
withdraw solvent from the gallbladder and discharge the
solvent back into the reservoir. The system further includes
a pump controller having an input terminal in communication
with the system bus and a plurality of output terminals, one
of said output terminals in communication with the aspiration
pump and one of said output terminals in communication with
the infusion pump, the microprocessor controlling said pump
controller, which in turn controls the aspiration and infusion
pumps in response to signals received from said pressure
transducer. The microprocessor terminates infusion and
initiates aspiration in response to signals indicating excess
pressure in the gallbladder.

Additionally, the system also includes a catheter having
a plurality of lumens, a first one of the lumens connected at
its proximal end to the infusion pump; a second one of the
lumens connected at its proximal end to the aspiration pump;
and a means to sense intra-gallbladder fluid pressure
associated with the distal portion of the catheter for
continuously providing an indication of the pressure of
fluid to the pressure transducer.

Yet another aspect of the invention is the ability to
safely dissolve gallstones when pressure measurements are
uncertain by infusing and aspirating intermittently a volume
of solvent which is less than the available volume of the
gallbladder.

BRIEF DESCRIPTION OF THE DRAWINGS
Figure 1 is a schematic diagram of an apparatus suitable for delivering solvent to a gallbladder and for removing the solvent containing dissolved or fragmented gallbladder stones. Figure 2 is a schematic diagram of a controller circuit that regulates the pump units shown in Figure 1, as well as other features of the apparatus.

Figures 3, 4 and 5 show features of a three-lumen catheter, Figure 3 being a sectional view taken on line 3-3 of Figure 4.

Figure 6 is a schematic diagram of another embodiment of the apparatus.

Figures 7 and 8 show features of another suitable three-lumen catheter, with Figure 8 being a sectional view taken on line 8-8 of Figure 7.

Figure 9 is a schematic diagram of an embodiment of the catheter portion of the invention in the form of a pigtail catheter, Figure 9A is a cross-sectional view of the catheter of Figure 9 taken through line 9A-9A.

Figure 10 is a block diagram of an embodiment of the apparatus wherein a microprocessor controls the components of the apparatus.

Figure 11 is a schematic diagram of the catheter of the invention positioned within the gall bladder of a patient.

Figure 12 is a flow diagram of an embodiment of the algorithm of the invention depicted in Figure 10. Figure 12A is a flow diagram of the start pumps subroutine of the algorithm of figure 12. Figure 12B is a flow diagram of the purge subroutine of figure 12. Figure 12C is a flow diagram of the alarm subroutine of figure 12. Figure 12D is a flow diagram of the check pressure limits subroutine of figure 12. Figure 12E is a flow diagram of the control pumps subroutine of figure 12.
DETAILED DESCRIPTION OF THE INVENTION

The invention described herein is suitably employed for delivering fluids (solvents) to organs for removing obstructions contained therein. It will be appreciated at the outset that, while the subject invention described below details the invention regarding the removal of gallstones from the gallbladder, the invention can be used to remove a variety of obstructions from bodily cavities or organs other than the gallbladder, and thus should not be construed as being narrowly limited to the treatment of gallstones. Indeed, it will become readily apparent that the device is easily adapted to removing obstructions from organs or bodily cavities in general.

The invention described herein is an organ pressure sensitive apparatus having a solvent delivery means in constant communication with a controller circuit via one or more pressure transducers that monitor the intra-organ pressure.

The pressure transducer may be positioned either within the gallbladder itself or external to the patient at the proximal end of a fluid filled column whose distal end is placed within the gallbladder. This can be accomplished by using the pressure sensing lumen either as the fluid filled column or as the in situ location of the pressure sensing transducer itself. A variety of pressure transducers are available for both in situ and fluid column use. In situ transducers need be small and capable of withstanding the effects of the solvent. Suitable transducers include but are not limited to fiber optic pressure sensors, piezoelectric pressure sensors and capacitative sensors. The wires or fibers of an in situ transducer pass through the separate pressure sensing lumen or through either of the solvent flow lumens or may be embedded in the catheter wall. A suitable
transducer for use on the proximal end of the fluid column is a Statham Gould pressure transducer P23ID. When using an in situ transducer, it is possible to have the transducer removable from and insertable into the catheter once the catheter is in position within the gallbladder. In this way, the transducer can be replaced during the procedure. Additionally, such an insertable transducer would permit the use of a smaller catheter for the same amount of fluid flow since it could be placed in one of the flow lumens. The apparatus functions over a preset pressure range delivering fluid to the gallbladder, causing the fluid to contact and dissolve the gallstones, and withdrawing fluid from the gallbladder, thereby accomplishing the removal of dissolved or fragmented gallstones. The rate of solvent delivery and removal can be adjusted to create the necessary turbulence to dissolve or fragment gallstones. If the pressure exceeds that of the normal operating range, the apparatus diverts solvent from the organ, thereby preventing leakage of the solvent from the site of treatment. Further, above the normal operating pressure range, the apparatus can be programmed to be "self-purging". This may be desirable in the instance when the obstruction is only partially dissolvable, causing blockage of the solvent removal or aspiration means. At pressures below the normal operating pressure range, the rate of aspiration is decreased while infusion continues, thereby reestablishing normal operating pressure.

Dissolution time is minimized by operation at high solvent flow rates. The maximum flow is attained when the instantaneous infusion flow matches the instantaneous aspiration flow. At such a null point, neither pump is slowed down or shut off by the pressure determining algorithm. A feature of this invention is the calibration of the pump catheter system in both infusion and aspiration, hence
generating a flow vs. control voltage relationship for both pumps. An input parameter is the desired flow rate. The microprocessor will not accept values which can not be attained by both pumps and operates both pumps at the desired flow rates when the pressure is in the vicinity of the pressure set point. As pressure rises above the set point the aspiration pump speed is increased and as the pressure falls below the set point the aspiration pump speed decreases thus possessing an ability to drive the system to the set point. During a procedure, the flow rate may be increased to a value limited by either the aspiration, or infusion lumen, or the size and compliance of the patient's gallbladder and/or the attendant pressure excursions experienced.

A key consideration with regard to the organ pressure-sensitive aspects of the system is the realization that leakage of solvent from the gallbladder occurs when the intraluminal pressure exceeds that in the cystic duct, common bile duct or ampulla (whichever is selected for the procedure in a particular patient) and that neither the gallbladder volume per se nor the flow rate of solvent per se are intimately involved. This in turn leads to recognition that critical leakage pressure from the gallbladder differs from patient to patient, and that leakage is a function not only of solvent delivery but natural gallbladder contractions or external pressures to the gallbladder. The subject invention takes into account those pressure changes that are of sufficient duration or strength to affect solvent leakage.

Because the critical leakage pressure from the gallbladder differs from patient to patient, it is important to determine the critical leakage pressure for each individual patient. To determine this pressure, a catheter is introduced into the gallbladder and, under fluoroscopy, a contrast material is injected into the gallbladder with increasing
pressure. The pressure at which the contrast medium enters the intestine or leaks at the percutaneous entry point is the critical leakage pressure. As the gallbladder fills, its pressure will increase until contrast medium is observed radiographically to flow through the cystic duct into the common bile duct or leak at the percutaneous entry site. The volume of dye present in the gallbladder at this pressure is the available volume. This critical leakage pressure, or a safety pressure below the critical leakage pressure, and, if desired, the available volume are entered as parameters in the controller. From the critical leakage pressure value, the high pressure or maximum operating point or upper set limit is determined.

Typically, the maximum operating pressure is set at 75% to 90% of the measured critical leakage pressure, and the maximum pressure alarm is typically 85%–95% of the critical leakage pressure.

To determine the minimum operating pressure or lower set limit, the contrast medium is aspirated from the gallbladder. As the pressure inside the gallbladder falls, bile will eventually begin being aspirated into the gallbladder from the common bile duct. The pressure at which this occurs is the bile aspiration pressure. The minimum operating pressure or lower set limit is typically set 2 to 10 cm of water above the bile aspiration pressure to minimize solvent dilution with bile. The minimum alarm pressure is set slightly below the bile aspiration pressure.

Accurate measurements of volumetric flow, to and from the gallbladder, will permit the calculation of net fluid retained in the patient. The signal of net volume of retained fluid can be used as a backup safety check when pressure measurements are controlling the pumps or as a primary control mode when pressure measurements are not possible, e.g., an
aberrant cystic duct, with no valves of Heister. To benefit
from volumetric flow measurements, pumping should be initiated
when the gallbladder is evacuated. When the net retained flow
approaches the predetermined gallbladder volume, an alarm
should be established or net aspiration should be increased.

Figure 1 shows an exemplary apparatus for removing
gallstones. Reservoir 10 contains a solvent that is a
chemical suitable for dissolving gallstones. Should the
gallstone be composed of cholesterol, a variety of solvents
would be efficacious. Particularly effective is methyl tert-
butyl ether (MTBE). The latter has been shown to readily
dissolve cholesterol stones rapidly both in vitro and in vivo.
At normal operating pressures, the solvent moves via a conduit
12 from the reservoir 10 by aid of a first pump 14. The fluid
then moves through a valve 16 and from the valve through
infusion port 17 in a catheter 19 into the gallbladder.
During this operation valve 26 is closed to prevent solvent
return to reservoir. The solvent is delivered at a
predetermined effective rate for gallstone dissolution thereby
providing solvent turbulence and contact with the gallstones
for a period of time sufficient for effective gallstone
dissolution or fragmentation and fragment removal.

Simultaneously with the delivery of MTBE to the
gallbladder, a second pump 18 aspirates the fluid from the
gallbladder now containing dissolved gallstones and debris.
This material passes out of the gallbladder via an aspiration
port 20 in the catheter. The fluid is pumped from the
gallbladder by pump 18, passing through valve 23, and from
there it is deposited in a receiver reservoir. Either
reservoir 10 used as the source of the solvent or a separate
reservoir is suitable for this purpose. Figure 1 shows the
same reservoir 10 being utilized as both the source of fluid
passed to the gallbladder and as the receiver of aspirated
fluid therefrom. It is worth noting that if the same reservoir is used, gallbladder stone fragments, bile, mucous and the like removed from the gallbladder are heavier than the solvent, MTBE, and therefore settle to the bottom of the reservoir and do not hinder continued withdrawal of essentially pure fluid from the reservoir to effect further stone dissolution.

In the case where a single reservoir is used to supply the solvent and receive the aspirated fluid, the fluid should be periodically sampled and the cholesterol concentration in the MTBE measured. Since the heavy debris falls to the bottom of the reservoir, the sample of the fluid should be taken of the fluid from the upper portion of the reservoir. The sample can then be tested to determine the cholesterol concentration level, for example by spectrophotometry. The fluid should be removed and replaced when the cholesterol concentration reaches a predetermined level (e.g. about 30%). It should be noted that higher or lower concentration levels of cholesterol in the solvent only effect the efficiency of dissolution.

Further, in a single reservoir system, since the aspiration rate and the infusion rate are in general not equal, there is a provision to vent the reservoir. The venting method should not allow the flammable fumes of the solvent to escape. An alternative way of compensating for rate differences is the use of a solvent resistant bladder for the reservoir. Such a bladder expands or contracts as the volume of fluid contained within it changes. This form of closed reservoir prevents fumes from escaping.

The pumps 14 and 18 are controlled by a controller circuit 22. The controller circuit 22 in turn receives pressure readings from the transducer 24 causing the controller circuit 22 to open or close flow valves 16, 23 and 26 to inhibit infusion or aspiration as necessary to control
organ pressure depending on whether the transducer 24 indicates that the pressure in the gallbladder is within, above, or below the normal operating pressure range. The transducer in turn senses the gallbladder fluid pressure by communication through port 28 of the catheter 19.

At the normal operating pressure, first pump 14 delivers fluid from reservoir 10 through tube 12 and valve 16 to the gallbladder. Simultaneously, and at a slightly slower rate, second pump 18 aspirates the fluid from the gallbladder through catheter aspiration port 20. Fluid passes through the valve 23 and thence through conduit 25 to the reservoir 10.

Conduit 12, catheter 19 and conduit 25 form a fluid circuit connecting the source reservoir 10 with the bodily organ or cavity into which the catheter is inserted and then to the receiving reservoir (which as noted may also be reservoir 10). The pumps 14 and 18 are in the circuit, in conduits 12 and 25 respectively. (For the purpose of description herein, the "forward" fluid flow direction will be defined as flow in the direction of the arrows in Figures 1 and 6, and "reverse" flow will be flow in the direction opposite the arrows.)

The controller 22 is programmed to respond to pressures that exceed or are below that of the normal operating pressure range. Above the normal operating pressure range ("high pressure mode"), the controller 22 shuts down valve 16 and simultaneously opens valve 26. This provides a path for diverting the incoming fluid away from the gallbladder. At that time valve 23 is open to continue gallbladder emptying to return the pressure to the normal operating range. If the pressure in the gallbladder does not return to the normal operating pressure setting within a preset time, for example a few seconds, then the controller 22 can be programmed to instruct the pumps to reverse the direction of fluid movement,
and simultaneously valves 23 and 26 are closed. The controller unit is programmed to close valve 23 after a slight delay so that a small amount of fluid, approximately 1 ml, can pass through the valve before it is shut. Valve 16 is opened to provide a path for fluid to be reverse aspirated from the gallbladder in this "self-purging" mode. This mode essentially causes a small amount of fluid to be pumped in through the aspiration port 20 of the catheter 19 to clear it of obstructions while aspiration is effected by pump 14 through valve 16. The fluid which is pumped into the gallbladder passes from the reservoir 10 through valve 23, prior to valve 23 closing in response to high pressure present in the gallbladder. Generally this will consist of about 1 ml of fluid passing through valve 23 before it shuts. This mode of operation continues for a brief period of time, and then the controller unit 22 instructs the machine to resume normal operation should the obstruction be removed and the pressure transducer 24 indicate reestablishment of the normal operating pressure range. If the transducer continues to indicate pressures present in the gallbladder above the normal operating pressure, the controller unit 22 again instructs the pumping apparatus to purge the system. If, after several "self purging" cycles, the obstruction is still not removed, the controller unit 22 then shuts down the system and activates an alarm circuit 34 notifying the user of a potentially dangerous condition.

Figure 2 illustrates a representative controller unit 22. The controller circuit 22 instructs the pumps 14 and 18 to deliver or aspirate fluid from the gallbladder. Thus, a circuit will typically have a pressure transducer 30; such as the Statham Gould pressure transducer P23ID, as mentioned previously. The pressure transducer 30 relays information to an amplification device 32 which amplifies the signal from the
transducer 30 and transmits it to a high and low pressure alarm circuit 34, then either directly or through the averaging circuit 36 to a pressure-sensing circuit 38 that reads preset low and high pressure values and which is connected to the valves 16, 23 and 26. The latter valves are typically solenoid flow valves or tube compression valves. The averaging circuit 36 can be switched in if desired to discriminate between pressure changes in the gallbladder arising from fluid build-up due to obstructions or from hyperventilating, laughing or like activities. Thus the averaging circuit essentially screens out artificially high or low pressure peaks which in fact do not lead to gallbladder emptying.

The pressure sensing circuit 38 is connected to a cascade timer 40, which in turn is connected to a pump reverse relay circuit 42. Thus, when gallbladder pressure exceeds that of the normal operating pressure range and the obstruction is not removed within a predetermined period, the cascade timer 40 activates the pump reverse relay 42. The latter circuit is responsible for "self-purging" the system. Should high pressure persist after several brief "self purging" cycles, then the alarm circuit 34 is activated, causing an initial period of aspiration in the reverse mode (with valves 16 and 23 open and valve 26 closed), then stopping the pumping system by shutting off its power supply and the triggering of a visual, audible or other alarm notifying the user. Note that at any time during the pump reverse cycle, should the pressure return to within the normal pressure range, the apparatus resumes normal operation.

It will be further noted as shown in Figure 2 that a pump power relay circuit 44 and a pump speed control circuit 46 are also interactive with the whole system. The pump speed control circuit 46 derives power through the pump power relay
44, which, in turn, is controlled by the alarm circuit 34. The pump motor derives its power supply from the pump power relay 44. Any time an alarm condition exists, this relay shuts off power to the pump, stopping it from pumping. The pump speed control circuit 46 has a manual adjustment capability through which the operator can set the desired perfusion rate for that specific situation. An analog pressure read-out 48 is provided for the operator to assess effective operation and to refer to during calibration. Alternatively, or in addition, the output can be fed to a video display terminal 118 (of Fig. 10) driven by appropriate software to provide the operator with an intermittent or continuous display of system operating mode, pressure, etc., and may be integrated with the indicators and alarm of alarm circuit 34.

Note that if desired, one or more appropriate microprocessors can replace many of the components of the system. Referring to Figure. 10, in a system controlled by a microprocessor 100, the microprocessor 100 is connected to the pressure transducer 24 by an analog to digital converter (A/D) 116 connected to the system bus 122. The A/D converter 116 changes the pressure transducer's 24 analog signals to digital signals for processing. Control of the pumps is accomplished by the microprocessor 100 through a digital/analog converter (D/A) 112, if the pump controller (PC) 124 requires analog signals, or through a digital parallel or serial interface (P/SI) 114 if the pump controller 124 is capable of responding to digital signals. The D/A 112 or the P/SI 114 can also be used to control the solenoid valves 16 (only one shown for purposes of illustration).

The digital data is processed by the microprocessor 100 which executes algorithms located in memory 110 to perform the functions otherwise performed by components of the pressure
sensing circuit shown in Fig. 2. Specifically, the
microprocessor 100 by itself replaces the high and low
pressure detector 34, the signal averager 36, and the cascade
timer 40. The microprocessor 100 in conjunction with the A/D
converter 116 replaces the pressure sensing portion of the
pressure sensing and solenoid control interface 38, while the
microprocessor 100 in conjunction with the D/A 112 or P/SI 114
replaces the solenoid portion of the pressure sensing and
solenoid control interface 38. Further, depending upon the
form of the controller 124 actually controlling the pumps 14,
18, the microprocessor 100 and A/D 116 or P/SI 114 also may
replace the pump power relay 44, speed control circuit 46, and
pump reverse relay 42.

Figure 6 illustrates another alternative embodiment of
the apparatus, which eliminates the valves by having separate
control of the two pumps 14 and 18. Each pump motor has its
own DC drive 47 and 45 respectively. Both drives are
controlled by controller 22', which has an appropriate
microprocessor to control the speed of each motor (and thus
the flow rate of each pump) in response to the pressure
signals from transducer 24. Thus instead of opening and
closing valves to effect the proper infusion, aspiration or
purging, the controller 22' regulates each pump's flow rate
and direction of flow.

This embodiment has the advantage that all fluid conduits
(tubing, catheter, reservoir) can be made of easily
replaceable material. Thus each patient can be treated using
a system in which all wettable surfaces are limited in use
solely to that one patient and one treating session. Again
many of the components of this embodiment can also be replaced
with a microprocessor system.

There are several features of the apparatus that enhance
its performance. The pumps preferred in the subject invention
are peristaltic pumps. This type of pump offers several
advantages such as the replaceable wettable surfaces mentioned
above, which in addition to their individual sterility will
be particularly advantageous in those instances where the
solvent being used to dissolve the obstruction is at all
corrosive. Moreover, peristaltic pumps are resistant to
clogging, in contrast to standard syringe type pumps.
However, it should be noted that syringe pumps are similarly
employable in the subject invention in those instances where
the fluid used to dissolve and remove the obstruction is a
solvent, provided that the syringe pumps are constructed of
suitable material, preferably polytetrafluoroethylene (PTFE)
or glass. Syringe pumps made of plastic are not preferred in
instances where the solvents used are incompatible with the
plastic composition of the syringe. An additional
disadvantage associated with the use of syringe pumps that is
not present in peristaltic pumps is that in those instances
where a solvent is being utilized, evaporation of the solvent
from between the plunger and the body can cause deposits in
the body of the syringe, causing it to "freeze" and thus
interrupt delivery of the fluid to the organ being treated.
Lastly, peristaltic pumps are capable of much greater fluid
circulation rates than are syringe pumps. This is
advantageous in certain instances where the obstruction to be
removed, such as a gallstone, requires turbulent flow rates
across the surface of the gallstone to accelerate the
dissolution process.

A predetermined normal operating pressure range is
programmed into the controller circuit 22. Should the
pressure in the gallbladder exceed normal operating pressure,
the action of the controller circuit 22 prevents leakage of
solvent from the gallbladder through the cystic duct into the
common duct, as well as into the intestine or around the entry
site of the catheter. Also, because the controller circuit "sees" true gallbladder pressure, it readily adjusts to decrease as well as increase pressure by adjusting the net delivery rate of the solvent to the gallbladder. For example, should the pressure fall below the normal operating pressure range, the controller circuit 22 ceases or slows down the rate of aspiration of solvent, and simultaneously continues infusing solvent to reestablish normal operating pressure.

The pressure sensitive alarm circuit 34 is constantly comparing the system's set operating pressures and the gallbladder pressure. If gallbladder pressure cannot be brought into the normal operating pressure range by the action of the controller circuit 22 in a specified period of time, it will revert to a period of maximal aspiration, then shut down the pumping system and sound an alarm drawing the attention of the operator. The operator, after correcting the problem, can resume normal operation by activating the reset button 49.

Referring to Figs. 10 and 12, in the case of a microprocessor system, the microprocessor 100 monitors the pressure values produced by the transducer 24 and controls the pumps 14, 18, and valves 16 in response to those pressure values according to an algorithm stored in the system memory 110. The algorithm can be generally partitioned into a module for periodically making pressure measurements, a module for controlling pump speed and direction and a module for determining the proper response to the various pressure measurements.

The module for determining the proper response to the various pressure measurements checks several conditions. If there are no variations of a predetermined amplitude in the measured pressure for a predetermined amount of time, the module assumes that either the pressure lumen is blocked or
that the pressure measurement subsystem has failed and sets
an alarm condition. The setting of an alarm condition causes
the pump control module to set maximal continuous aspiration
by both pumps and to sound an alarm.

If the pressure measured is greater than the upper set
limit, the pressure measuring module instructs the pump
control module to stop the infusion pump and cause the
aspiration pump to maintain aspiration. If the pressure
continues to remain above the upper set limit for more than
a predetermined amount of time, the module assumes that there
is a blockage in the aspiration openings or lumen. In
response to this condition, the pump control module instructs
the pump normally used for infusion to aspirate. When the
pressure falls to the lower set limit, the pump control module
instructs the pump normally used for aspiration to switch to
infusion and the pump normally used for infusion to switch to
aspiration in an attempt to purge the side holes and lumen.
If the operating pressure does not return to normal within a
predetermined amount of time or after a predetermined volume
has been used to purge the aspiration openings and lumen, an
alarm condition is set by the response determination module.
Further, if there are more than a predetermined number of
purge cycles within a predetermined period of time, the
response determination module sets an alarm condition.

If the pressure measured is less than the lower set
limit, aspiration is stopped, and if the pressure remains less
than the lower set limit for a predetermined amount of time,
an alarm condition is set. Finally, if the system is unable
to operate within its normal range for a predetermined amount
of time, an alarm condition is also set.

Figure 12 is a flow diagram of the main program loop of
an embodiment of the algorithm used to determine the proper
response to various pressure measurements. Figures 12A-12E
are flow diagrams of subroutines executed during the main program loop. The main program calls the CHECK-PRESSURE-LIMITS subroutine 150 which in turn calls a series of other subroutines to perform specific functions when the pressures and/or time delays are outside the desired ranges, and when the pressure is above the upper pressure limit or below the lower pressure limit. Within the desired pressure range, the CONTROL PUMPS subroutine 152 operates the pumps in a proportional fashion in an attempt to stay within the pressure limits. The main program begins by the operator entering the operating parameters (operating pressures, alarm pressures, etc.) into the system by the system keyboard and then calling the START-PUMPS subroutine 149.

When the main program is executed for the first time during the procedure, or when the pumps have been stopped and must be restarted the subroutine START-PUMPS is called. Referring to Figure 12A, the purpose of the START-PUMPS subroutine is to determine from the present pressure measurement which pump should be started. That is, if the pressure is high initially, only aspiration should occur, while if the pressure is low only infusion should occur. Further, should the system be unable to come to the proper pressure operating range within a fixed amount of time, an alarm condition exists and the operator should be notified. To accomplish this, the subroutine begins by determining if the pressure in the gallbladder is greater than the lower operating pressure limit 160 and if the pressure is not greater, then the infusion pump is turned on and the aspiration pump remains off 166. If the pressure is greater, the infusion pump remains off, the aspiration pump is turned on 162, an aspiration timer is started, and the pressure is compared to the lower operating pressure limit again 163. If the pressure is still above the lower operating limit 163, the
elapsed time from the start of aspiration as indicated by the aspiration timer is compared 164 to the maximum aspiration time allowed parameter. If the elapsed time is less than the maximum aspiration time allowed, the pressure is again compared with the lower operating pressure limit 163. If the elapsed time is greater than the maximum allowed then aspiration has failed to reduce the pressure and the alarm subroutine is called in an alarm (0) condition 165.

If the pressure is below the lower operating pressure limit 163, the infusion pump is turned on, the aspiration pump is turned off, the aspiration timer is cleared, an infusion timer is started and the pressure compared to the upper operating pressure limit 168. If the pressure is less than the upper operating pressure the elapsed time of infusion is compared to the maximum infusion time parameter 176. If the elapsed time is greater than the allowed time 176, indicating a leakage of solvent out of the gallbladder, the alarm subroutine is called in an alarm (0) condition 178.

If the pressure is greater than the upper operating pressure limit, the infusion pump is turned off, the aspiration pump is turned on, the infusion timer is cleared, and the aspiration timer is again started. The pressure is again compared to the lower operating limit 184 and if it is less than the lower operating limit, the aspiration timer is cleared, the infusion pump is turned on and the aspiration pump is turned off 187.

If the pressure exceeds the lower operating pressure limit 184, the aspiration timer is compared to the maximum aspiration time parameter 186 and if the elapsed time exceeds the maximum time allowed, indicating that aspiration is unable to reduce the pressure, the alarm subroutine is called in the alarm (0) condition. If the elapsed time is less than the maximum aspiration time, the pressure comparison cycle is
repeated 184.

Once the infusion pump is on and the aspiration pump is off 187, the pressure is compared to the operating set pressure 189 and if it is less, the pressure comparison loop is repeated. If the pressure exceeds the operating point the subroutine simply returns to the main routine.

When the it is determined that the aspiration pump is unable to aspirate sufficiently to maintain pressure within the requisite range below the upper pressure limit, the CHECK PRESSURE subroutine causes both pumps to maximally aspirate, and if the lower pressure limit can be attained and the allowed number of purges have not been exceeded 314, 326, 328, 322 and 330 of Fig. 12D, it is assumed that the aspiration port is blocked and that a purge should be attempted. The PURGE subroutine is called to reverse flow through the aspiration and infusion lumens in an attempt to clear the aspiration lumen. Referring to Figure 12B, the PURGE subroutine first starts a purge timer 196, and sets both the infusion and aspiration pumps in reverse 192, 194 at the set flow rates in an attempt to clear the aspiration lumen. The elapsed time from the purge timer is compared 196 to the purge cycle period, and the purge cycle is allowed to continue if the elapsed time indicated by the purge timer is less than the purge cycle period and the pressure of the fluid in the gallbladder is less than the upper operating pressure limit parameter 198. If the pressure is less than the upper operating pressure limit, the purge continues and the elapsed time compared 196 again. If the pressure exceeds the upper pressure limit 198, the program will proceed through decision point 200, and the pressure check subroutine which will cause maximum aspiration and another purge cycle again if the number of purge cycles has not been exceeded.

If the purge cycle time is exceeded without exceeding the
upper pressure limit, the pressure is compared to the operating set point 200. If the pressure is below the set point, the aspiration pump is stopped 202, and the infusion pump is operated at set point in the forward direction. If the pressure does not attain the operating set point 206 within the maximum infusion time, the system calls alarm subroutine 212 in an alarm (1) state. If the operating set point is attained within the time parameter 210, the system returns to the operate cycle through 224 and 226.

If, upon the completion of time 196, the pressure is above the set point, the infusion and aspiration pumps are turned on in the forward direction 224, 226 and the program returns to the operate cycle.

There are two alarm conditions depending upon whether an abnormal pressure condition is recoverable (alarm (1) condition) or whether the condition is so hazardous that normal operation should not be resumed (alarm (0) condition). In either case the first priority is to aspirate from both lumen to reduce the pressure. If the lower pressure limit can be attained within the alarm aspiration time, an alarm (1) condition occurs and normal operations are resumed. If the condition is an alarm (0), a warning is given and the operator must intervene to stop aspiration. Referring to Fig. 12C, the ALARM subroutine, is entered in one of two states: alarm (0) 252, and alarm (1) 250. In either state, the infusion pump is set to maximum reverse 254, 256 while the aspiration pump is set to maximum forward 258, 260 to generate maximum aspiration. If the alarm (0) state 252 was entered, a tone is set 266, and aspiration is continued until the pumps are stopped by operator intervention 270. No further pumping occurs until the pumps are manually restarted 274.

If the alarm (1) state 250 was entered, a timer is started and the pressure is compare to the lower operating
pressure and if it is less than the lower operating pressure, the pumps are set to operate normally, infusing fluid 268 through the infusion lumen and aspirating fluid 272 from the aspiration lumen. If the pressure is above the lower operating pressure, the elapsed time of maximum aspiration is compared to a parameter which determines the maximum time allowable at maximum aspiration and if that time has not been reached the pressure is compared again 262. If the elapsed time exceeds the maximum time allowed, a tone is set 266, the pumps continue to aspirate at maximum rate until they are stopped 270 by manual intervention. No pumping commences until the pumps are restarted manually 274.

The CHECK-PRESSURE-LIMITS subroutine is called by the main routine to determine the proper response to the current pressure. Referring to figure 12D, the CHECK-PRESSURE-LIMITS subroutine begins by starting a timer to measure elapsed time and calculating the pressure change in the last three seconds. If the pressure change is less than 1 torr, it is assumed that the pressure transducer is not operating correctly and the alarm subroutine is called in the alarm (0) state. If the pressure change is greater than 1 torr, the pressure is compared to the minimum alarm pressure 304 and if the pressure is less than the minimum alarm pressure, the elapsed time indicated by the timer is compared to the minimum alarm pressure trigger time parameter 306. If the time is greater than the minimum alarm pressure trigger time, then, the pressure has been below the minimum allowable pressure for too long, and the alarm subroutine is called in the alarm (0) state. If the time is less than the minimum pressure alarm trigger time, the pressure is compared 310 to the maximum alarm pressure and if it is less the maximum alarm pressure is compared to the upper pressure limit 318.

In either case, the elapsed time is compared to the upper
pressure alarm trigger time 312 or upper pressure delay time
320 and if the upper pressure alarm trigger time is exceeded,
the number of purges is compared to the number allowed 314 and
if too many purges have occurred, the alarm subroutine is
called in the alarm (0) state 316.

If the number of purges has not been exceeded, the
aspirate pump is set to maximum flow 326. The infusion pump
is reversed and set to maximum flow 328, and the counter of
the number of purges is incremented. The pressure is then
compared to the lower pressure limit 322. If the pressure is
below the lower limit within the alarm aspiration time 324 a
purge cycle is performed 330, if not the alarm subroutine is
called 332 in an alarm (0) state.

If the pressure is below the alarm pressure 310 and the
upper pressure limit 318, the pressures are within the desired
limits and the system returns to the operate cycle.

When the pressure is below the upper limit and above the
lower limit, the CONTROL PUMPS subroutine controls the pumps.
Referring to the Fig. 12E, the infusion pump will operate until
the upper limit is attained 340, 342. The aspiration pump is
turned off upon the attainment of the lower limit 346, 352.
At pressures between the lower limit and 85% of the set point
pressure, the aspiration pump operates at 80% of set flow,
348, 354. At pressures between 115% of set pressure and the
upper pressure limit, the aspiration pump operates at 200% of
set flow, or maximum flow whichever is lower 350, 356. When
the pressure is ±15% of the set pressure, both pumps operate
at set flow 358, 344.

The apparatus is completely automatic and is operable
without any significant operator input beyond the critical
pressure and available volume. Moreover, it is readily
converted to a completely closed circuit system in those
instances where the therapeutic fluid is combustible. This
feature is required for particularly combustible solvents. Any of a number of types of tubing is suitably used with the pumps of the subject apparatus. However, we have found that tubing composed of "Tygon Special Formulation F-4040A" (a vinyl material) or "Nalgene" (a polyurethane) is particularly compatible with solvents such as methyl tert-butyl ether. Moreover, tubing with a large internal diameter is favored for use with peristaltic pumps, enabling a high volume per revolution ratio to be obtained, thereby permitting a low revolution per minute rate to be utilized, hence minimizing torque build-up when a switch over to the high pressure mode leads to pump motor reverse.

As discussed above, the subject apparatus can be utilized for removing obstructions in a variety of organs. However, in the instance where it is used to remove gallstones from gallbladders, perfusion rates of about 50 ml/min to 300 ml/min are generally more effective. This is readily accomplished by manually adjusting the pump speed control circuit 46 of Fig. 2. It is important that the flow rate is sufficient to cause turbulent flow within the gallbladder. It has been found that turbulence increases the rate of gallstone dissolution and helps in removing the non-dissolving fragments.

A variety of catheters usable to deliver and aspirate the fluid can be suitably employed. The catheter must be insoluble in the solvent being infused. For example, a polyurethane catheter is suitable for use with MTBE. Three-lumen catheters as shown in Figures 3-5 and 7-8 are favored since pressure measurements as well as perfusion and aspiration of the fluid can all be carried out simultaneously. A suitable three-lumen catheter should have an outside diameter not larger than can be readily employed for the surgical insertion of the catheter into the gallbladder, and
should have an aspiration lumen 50, a pressure sensing lumen 52 and an infusion lumen 54. The aspiration lumen preferably should be larger in cross-section than the other two lumen. For the purpose of safety, while achieving effective flow in the system, the aspiration cross-sectional area should be about 2.5 times the infusion cross-sectional area. In this way, the volume removed by aspiration can be greater than the volume replaced by infusion under emergency conditions, while allowing a substantial flow to be maintained through the infusion lumen.

Each lumen communicates with the gallbladder through a number of openings in the outside wall of the lumen. The sum of the cross-sectional areas of openings to a lumen should be greater than the cross-sectional area of that lumen in order to minimize flow impedance. The cross-sectional area of each opening should be less than the cross-sectional area of its lumen to prevent debris from obstructing the lumen. The aspiration and infusion openings are distributed along the length of the distal end of the catheter. At least one aspiration opening is located proximal to all infusion openings, preferably being located at the entry point of the catheter into the gallbladder when the catheter is in position for operation. With this configuration, aspiration takes place nearest the insertion point of the catheter into the gallbladder. Any leakage of solvent from the gallbladder through the entry point of the catheter is therefore immediately aspirated and does not damage surrounding tissues.

The aspiration lumen extends to the distal end of the catheter and terminates in an opening at the distal end. Referring to Fig. 11, this opening in the distal end of the catheter also serves as a passageway through which a guidewire can pass. Note that the number of openings is not invariant, depending on the number of gallstones present in the
gallbladder, as well as the desirable therapeutic need to
effect rapid treatment.

The distal end of the catheter is preferably curved into
a pigtail shape as shown in Figure 7 to aid in its being
retained and positioned in the organ. Referring to Figs. 9
and 9A, such a pig-tailed catheter can also include a string
74 which helps the catheter retain its pig-tailed shape since
fluid being pumped through the catheter and patient movement,
coughing or sneezing tends to cause the catheter to unwind.
A monofilament or wire can be used in place of a string. The
retaining string can either pass through an opening 72 to its
own lumen 70 or can pass through the aspiration 50" or
infusion 54" lumen. Other means to retain the catheter within
the gallbladder are possible. For example, a balloon catheter
for example may serve to retain the catheter.

Since the string 74 may pass through its own lumen 52,
and since a balloon catheter generally also requires its own
lumen, the system should not be construed as being limited to
a three-lumen catheter. A variety of catheters of different
lumens will perform satisfactorily provided that the system
is modified to accommodate such catheters, such modifications
being well known to those skilled in the art.

When a pig-tailed catheter is used, openings to the
pressure lumen should be located on the inner radius of the
curve. This location provides a clear opening for accurate
pressure sensing and prevents the mucosa of the gallbladder
from interfering with the pressure measurements.

Because this procedure can be inherently dangerous, using
toxic and flammable solvents, it is desired that the catheter
be used only with the proper pumping system. To assure this,
the catheter can have a structural, electrical or fiberoptic
connection at its proximal end which is connectable to a
similar structure in the remainder of the system. The system
may therefore be prevented from functioning with an inappropriate catheter.

It will be appreciated by those skilled in the art that there are numerous modifications in the electrical circuitry, and the overall interconnecting features of the invention that will achieve the efficacious removal of obstructions in particular organs. For instance, while the automatic "self purging" feature of the apparatus is desirable, a device without this feature will perform adequately. Moreover, it should be further noted that, while the invention has been described as applicable to the removal of gallstones from gallbladders, its use should not be so narrowly construed. Thus, it is the intent herein to present an invention that is generally applicable for the removal of obstructions from a variety of organs by dissolving and dislodging the obstruction using solvents.

What is claimed is:
CLAIMS

1. A catheter for the contact dissolution of gallstones having, in generally side-by-side relationship, a solvent infusion lumen and a solvent aspiration lumen, the catheter sized for entry of its distal portion into the gallbladder from outside the body, each lumen having at least one opening in said distal portion for communication between the gallbladder and a remotely located pump means, the aspiration lumen having a greater flow cross-section than the infusion lumen; and means to sense intra gallbladder fluid pressure associated with said distal portion of the catheter for continuously sensing the pressure of fluid within said gall bladder, and transmitting an indication thereof proximally, for control of infusion and aspiration of solvents via said lumens.

2. The catheter of claim 1 wherein the cross-sectional area of said aspiration lumen is larger than the cross-sectional area of said infusion lumen.

3. The catheter of claim 2 wherein the ratio of the cross-sectional area of said aspiration lumen to the cross-sectional area of said infusion lumen is at least 1.5.

4. The catheter of claim 1 wherein the area of each opening is less than the cross-sectional area of the lumen with which said opening is in communication.

5. The catheter of claim 1 wherein the catheter further includes a retention means to prevent said catheter from being removed from said gallbladder.
6. The catheter of claim 5 wherein said retention means is a curved formation of said distal portion of said catheter.

7. The catheter of claim 6 wherein said pressure sensing means is located to lie at the inner radius of said curved formation to prevent its blockage by mucosa of the gallbladder.

8. The catheter of claim 5 wherein said retention means is an inflatable balloon located adjacent to said distal portion.

9. The catheter of claim 1 wherein the catheter further comprises a tension string for holding said distal portion of said catheter in a pigtail configuration.

10. The catheter of claim 9 further comprising a string passage lumen in which said string is located.

11. The catheter of claim 9 wherein said string is located in one of said aspiration lumen or said infusion lumen.

12. The catheter of claim 1 further comprising an aspiration opening at the distal end of the catheter in communication with said aspiration lumen.

13. The catheter of claim 1 or 12 having at least one aspiration opening in the wall of the catheter in communication with said aspiration lumen located proximal to all infusion openings.
14. The catheter of claim 13 wherein said proximally-located aspiration opening is located adjacent to the point of entry of the catheter into the gall bladder when the catheter is in position for operation.

15. The catheter of claim 12 wherein said aspiration lumen and aspiration opening at said distal end of said lumen are constructed and arranged to enable the catheter to pass over a guide wire.

16. The catheter of claim 1 wherein the catheter comprises a material which is resistant to the solvent to be infused into said gallbladder.

17. The catheter of claim 16 wherein the material is polyurethane.

18. The catheter of claim 1 wherein said means for sensing the pressure of fluid within the gallbladder comprises a third fluid pressure transmitting lumen extending side by side with said infusion and aspiration lumens and having a distal opening in said distal portion of said catheter, said lumen constructed to communicate intra-gallbladder pressure to a remotely located pressure transducer.

19. The catheter of claim 1 wherein said means for sensing the pressure of fluid within the gallbladder comprises a pressure transducer located in said distal portion of said catheter.

20. The catheter of claim 19 wherein said transducer is piezoelectric.
21. The catheter of claim 19 wherein said transducer is fiberoptic.

22. The catheter of claim 19 wherein the transducer is removably inserted in a lumen of the catheter.

23. The catheter of claim 1 wherein the catheter has a structural formation at its proximal end that permits it to be used only with a solvent delivery system having a predetermined mating structural formation that prevents inadvertent use with non-mating systems.

24. The catheter of claim 1 wherein the catheter has an electrical formation at its proximal end that permits it to be used only with a solvent delivery system having a predetermined mating electrical formation that prevents inadvertent use with non-mating systems but use fiberoptic rather than electrical.

25. The catheter of claim 1 wherein the catheter has a structural formation at its proximal end that permits it to be used only with a solvent delivery system having a predetermined mating structural formation that prevents inadvertent use with non-mating systems.

26. An apparatus for use in the dissolution of gallstones comprising:

   a microprocessor adapted to execute an algorithm comprising:
   a gallbladder pressure determining module to determine the pressure within the gallbladder of a patient in response to an input pressure signal derived from the gall bladder;
a pump control module to control the speed and
direction of an infusion pump pumping solvent through an
infusion lumen into and an aspiration pump pumping solvent
through an aspiration lumen out of the gallbladder of the
patient; and

a response determination module to control the
functions of the pump control module in response to the
pressure determinations of the pressure determining module.

27. The apparatus of claim 26 wherein said gallbladder
pressure determining module,
generates an alarm and initiates maximal continuous
aspiration by both infusion and aspiration pumps in response
to one of the set of conditions comprising:

no pressure variations of a predetermined amplitude
for a predetermined amount of time;

pressure does not return to a normal range within a
predetermined amount of time or after a
predetermined volume has been used to purge
said aspiration lumen;

more than a predetermined number of purge cycles
occurring within a predetermined period of
time;

pressure remains less than a lower set limit for a
predetermined amount of time;

system is unable to maintain the pressure within
normal range for a predetermined amount of
time;

stops infusion and maintains maximal aspiration in
response to the condition of the pressure exceeding an upper
set limit;

aspirates through infusion lumen until the pressure falls
to the lower set limit and then infuses 1-2 ml. through
aspiration lumen in response to the condition of pressure remaining above the upper set limit for more than a predetermined amount of time; and
stops aspiration in response to the condition wherein the pressure is less than the lower set limit.

28. An apparatus for dissolution of gallstones comprising:
a means for continuously measuring the pressure within the gallbladder of a patient; and
a means for controlling the infusion and aspiration of a solvent into the gallbladder in response to those measurements.

29. A method for dissolution of gallstones comprising the steps of:
continuously measuring the pressure within the gallbladder of a patient; and
controlling the infusion and aspiration of a solvent into the gallbladder in response to those measurements.

30. The method of dissolution of gallstones of claim 29, further comprising the step of periodically measuring the amount of cholesterol in the solvent.

31. The method of claim 30 wherein the solvent is replaced when the cholesterol concentration in the solvent reaches a predetermined concentration limit.

32. The method of claim 31 wherein the limit is about 30%.
34. The method of claim 33 wherein the step of measuring the critical pressure comprises the injection into the gallbladder of a radiopaque dye at increasing pressure until the discharge of said dye is observed radiographically.

35. The method of dissolution of gallstones of claim 29 wherein the step of infusing the solvent into the gallbladder occurs at a rate sufficient to create turbulence adjacent the gallstones.

36. An apparatus for the dissolution of gallstones comprising:
   a system bus;
   a microprocessor in communication with said system bus;
   a memory for holding algorithms, said memory in communication with said system bus;
   an analog to digital converter having an input terminal for receiving an analog signal representative of the intragallbladder pressure and an output terminal for applying digital signals representing said pressure on said system bus;
   a pressure transducer having a pressure sensor and an output terminal, said output terminal of said pressure transducer in communication with the input terminal of said analog to digital converter, said pressure transducer generating a pressure signal related to the pressure of the solvent within the gallbladder;
a reservoir for filling with a gall stone dissolving solvent;

an infusion pump connected by conduits to pump solvent from said reservoir into said gallbladder

an aspiration pump connected by conduits to withdraw solvent from the gall bladder and discharge the solvent into said reservoir;

a pump controller having an input terminal in communication with said system bus and a plurality of output terminals, one of said output terminals in communication with said aspiration pump and one of said output terminals in communication with said infusion pump,

said microprocessor controlling said controller, which in turn controls said aspiration and infusion pumps in response to signals received from said pressure transducer, said microprocessor terminating infusion and initiating aspiration in response to signals indicating excess pressure in the gallbladder; and

da catheter having a plurality of lumens,

a first one of said lumens connected at its proximal end to said infusion pump;

a second one of said lumens connected at its proximal end to said aspiration pump; and

a means to sense intra-gallbladder fluid pressure associated with said distal portion of the catheter for continuously providing an indication of the pressure of fluid to said pressure transducer;

the distal end of said catheter for placement within the gall bladder of a patient.

37. The apparatus of claim 36 wherein said reservoir is a collapsible bladder.
A catheter for the contact dissolution of gallstones having, in generally side-by-side relationship, a solvent infusion lumen and a solvent aspiration lumen, the catheter sized for entry of its distal portion into the gallbladder from outside the body, each lumen having at least one opening in said distal portion for communication between the gallbladder and a remotely located pump means, the aspiration lumen having a greater flow cross-section than the infusion lumen; and means to sense intra gallbladder fluid pressure associated with said distal portion of the catheter for continuously sensing the pressure of fluid within said gall bladder, and transmitting an indication thereof proximally, for control of infusion and aspiration of solvents via said lumens.
FIG. 12

START PUMPS

OPERATE CYCLE

CHECK PRESSURE LIMITS

CONTROL PUMPS

SUBSTITUTE SHEET
BOTH PUMPS OFF

P > P_{LL} YES INFUSE OFF ASPIRATE ON

NO

P > P_{LL} YES

NO t > t_{MAXASP} YES ALARM (0)

NO

INFUSE ON ASPIRATE OFF

P < P_{UL} YES

NO t > t_{MAXINF} YES ALARM (0)

NO

INFUSE OFF ASPIRATE ON

P > P_{LL} YES

NO t > t_{MAXASP} YES ALARM (0)

NO

INFUSE ON ASPIRATE OFF

P < P_{OP} YES

NO OPERATE CYCLE
PURGE CYCLE

INFUSE ON SET FLOW-REVERSE 192

ASPIRATE ON SET FLOW-REVERSE 194

196: t > t_{PURGE} NO 198: P > P_{UL} NO
YES

200: P < P_{OP} YES
NO

ASPIRATE OFF

INFUSE ON SET FLOW-FORWARD 200

INFUSE ON SET FLOW-FORWARD 224

ASPIRATE ON SET FLOW-FORWARD 226

OPERATE CYCLE

FIG. 12B

210: t > t_{MAXINF} YES
NO

212: ALARM (1)

214: P < P_0 NO
YES

202

204

206
**INTERNATIONAL SEARCH REPORT**

**I. CLASSIFICATION OF SUBJECT MATTER**

According to International Patent Classification (IPC) or to both National Classification and IPC

**US: 604/28 IPC: A61 M 1/00**

**II. FIELDS SEARCHED**

Minimum Documentation Searched:

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<th>Classification System</th>
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<td>US 604/27-35 43,49,50,65-67,118-119,151-152,244-246,276 128/DIG12, DIG13</td>
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Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched:

**III. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<tr>
<th>Category</th>
<th>Citation of Document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to Claim No.</th>
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<tr>
<td>Y,P</td>
<td>US,A, 4902276 (ZAKKO) 20 FEBRUARY 1990 SEE ENTIRE REFERENCE</td>
<td>26-35</td>
</tr>
<tr>
<td>Y</td>
<td>US,A, 4573966 (WEIKL ET AL.) 04 MARCH 1986 SEE FIGURES 1,2; COLUMNS 3 AND 4</td>
<td>1-4, 12-15</td>
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<tr>
<td>Y</td>
<td>US,A, 4777951 (CRIBIER ET AL.) 18 OCTOBER 1988 SEE FIGURES 1,1a,4a,9a and 9-12 (FITTAIL GATHERER)</td>
<td>6,7</td>
</tr>
<tr>
<td>Y</td>
<td>US,A, 4781677 (WILCOX) 01 NOVEMBER 1988 SEE ENTIRE REFERENCE</td>
<td>1-4, 12-15</td>
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<tr>
<td>Y</td>
<td>US,A, 4364394 (WILKINSON) 21 DECEMBER 1982 SEE FIGURES 2-4, 7 AND COLUMN 2, LINES 31-48</td>
<td>1-4, 12-15</td>
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**IV. CERTIFICATION**

Date of Actual Completion of the International Search: 15 MAY 1991

Date of Mailing of this International Search Report: 06 JUN 1991

International Searching Authority: ISA/US

Signature of Authorized Officer: NGUYEN

For C. SMITH

INTERNATIONAL DIVISION

Form PCT/ISA/210 (second sheet) (May 1988)
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<td>Y</td>
<td>US, A 4642092 (MOSS) 10 FEBRUARY 1987 SEE FIGURES 1 AND 3</td>
<td>1-8, 12-15</td>
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<tr>
<td>Y</td>
<td>US, A 4655744 (THISTLE ET AL.) 07 APRIL 1987 SEE ABSTRACT, COLUMN 2 LINES 10-56</td>
<td>26-35</td>
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<tr>
<td>Y</td>
<td>US, A 4180074 (MURRAY ET AL.) 25 DECEMBER 1979 SEE ENTIRE REFERENCE</td>
<td>26-35</td>
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<td>Y</td>
<td>US, A 3920014 (BANKO) 18 NOVEMBER 1975 SEE FIGURES 2, 3 AND COLUMN 3 LINE 24 -</td>
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<td>COLUMN 5, LINE 68</td>
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<td>Y</td>
<td>US, A 3860000 (WOOTEN ET AL.) 14 JANUARY 1975 SEE FIGURE 1, AND COLUMN 1, LINE</td>
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<td>30-COLUMN 2 LINE 12</td>
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<td>Y</td>
<td>WO, A 89/03230 (DAVIS) 20 APRIL 1989 SEE FIGURE 1 AND PAGES 5-6 AND PAGES 7-8</td>
<td>26-35</td>
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<td>X</td>
<td>US, A 4329994 (COOPER) 18 MAY 1982 SEE ABSTRACT; FIGURES 4-6 AND 9-10; AND</td>
<td>1-5, 8, 12-25</td>
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<td>COLUMNS 1-2; COLUMNS 5-6</td>
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<td>Y</td>
<td>US, A 4723556 (SUSSMAN) 09 FEBRUARY 1988 SEE COLUMN 1, LINES 50-53; COLUMN 2, LINES 13-29; AND COLUMN 3, LINE 50-66</td>
<td>18-25</td>
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