Out Came Copious Water

At 5:45 PM on Monday, March 26, 1827, Ludwig van Beethoven died in hepatic coma. During a violent thunderstorm with snow flurries and hail, a flash of lightning accompanied by a violent clap of thunder fell from the heavens and bathed the dying man’s room in a sharp light. If a friend’s recollection 30 years later is faithful, Beethoven opened his eyes for the first time in two days, raised his right hand in a clenched fist and stared up to the heavens with a grim and threatening look on his face, and then expired. Thus passed the Titan of western music, who once wrote to his friend and first doctor, Franz Wegeler, that “he wanted to seize fate by the throat,” —and he did.

In contrast to the inherently polyphonic disciplines of Cardiology and Pulmonary Medicine, Hepatology does not ordinarily come to mind as a particularly musical calling, unless one takes stock of our liberal use of percussion and the rare presentation of Cruveilhier’s and Baumgarten’s hum. Notwithstanding, Beethoven’s last performance is of especial hepatologic interest, not only because he had autopsy-proven cirrhosis (for which causes such as alcoholism, hemachromatosis, and primary sclerosing cholangitis have been proffered), but because he was undoubtedly the most celebrated patient to have undergone repeated large-volume paracentesis. In fact, between December 20, 1826 and February 27, 1827 Beethoven was “tapped” by surgical incision and glass tube insertion, without analgesia, no less than four times, resulting in the removal of upwards of 20 L per session followed by inexorable losses into the bed, the mattress, sheets and straw, and into wooden pails placed on the floor so that the water would not run in the room. Beethoven’s plight in his last few weeks was pitiable, relieved temporarily only by the paracenteses and his permitted indulgence in some fine wines and frozen alcoholic punch. The treatment Beethoven was given for ascites had been accepted and current for over 2,000 years; contrapuntally, the dramatic controversies in the 20th century about both the pathophysiology and the treatment of ascites seemed at times operatic.

The term ascites appeared in English (aschytes) in the late 14th century, taken from the Greek for dropsy, askitos (ἀσκίτης), itself derived from askos (ἀσκός), an ancient Greek word meaning a leather bag or a sheepskin used for carrying water, wine, oil, etc. Hippocrates (c.400 BC) observed that “when the liver is full of fluid and this overflows into the peritoneal cavity, so that the belly becomes full of water, death follows,” and thus, he must be credited with a combined version of the overflow and underfill hypotheses of ascites. Erasistratus of Alexandria (c.300 BC) also knew that “hardness of the liver” was a risk factor for ascites formation but, regardless of our Hippocratic reverence, it would be hypocritical not to acknowledge that the association between ascites and liver disease was previously recognized in the texts of the Ayurveda, the ancient Hindu system of medicine drawn from Vedic literature, and in the papyrus Ebers (c.1600 BC) of ancient Egypt. The ancient Mayans also knew of the association between tense ascites and umbilical herniation, as depicted in figures that have survived the conquistadors. On the other hand, the correlation between adultery and abdominal dropsy that was proposed in the Old Testament, remains unsubstantiated. Aulus Cornelius Celsus (30 BC–50 AD) is credited with the first detailed description of therapeutic paracentesis, including the recommendation to use a flanged bronze or lead tube for drainage while, in the 17th century, Sanctorius Sanctorius of Padua, Italy, designed the first trocar specifically for paracentesis. By the first half of the 20th century, the practice of paracentesis that started as a trickle at the beginning of a prior millennium, had swelled to a flood with the establishment in many major hospitals of “paracentesis clinics,” to which patients would return habitually for repeated drainage in the company of their equally fluid-
challenged peers. In what sounds like an opportunity for
an oratorio, Beethoven voiced relief after his first paracen-
tesis by likening the gush of his ascites to the water that
issued forth when biblical Moses knocked the rock.12

“And Moses raised his hand and struck the rock twice
with his rod. Out came copious water. . .”

Prior to the introduction of safe diuretics, large-vol-
ume paracentesis was the mainstay of therapy for cirrh-
ic ascites, much to the relief of the patient, the bravado of
the physician, and the horticultural benefit of many a rose
bush that bloomed better when fertilized with ascites.
One practitioner even boasted of his skill in hydraulics by
reporting the performance of no fewer than 69 2-imperial
gallon paracenteses in the same patient over a 4-year in-
terval.13 However, by the late 1950s the tide was turning,
so to speak, against large-volume paracentesis. Thia-
zides14 and spironolactone15 were introduced that to-
gether with low sodium diets,16 proved effective in
treating the majority of patients with hepatic ascites. The
availability of effective medical therapy along with reports
of the deleterious effects of large-volume drainage led to
the abandonment by all but a few stalwarts,17 of a proce-

sion (now obsolete) were devised,21 such as omentoplexy, ne-

phrectomy, and anastomosis of the renal pelvis to the
peri toneal cavity (thereby creating a peritoneovenous con-
duit), and even the implantation within the abdominal
wall of a hollow glass button that allows ascites to seep
into the subcutaneous tissues for absorption and recy-
cling. End-to-side portacaval shunts that very effectively
abolish ascites by reducing hepatic sinusoidal hyperten-
sion22 were also abandoned because of high operative
mortality and an unacceptable frequency of postoperative
encephalopathy. In this context, we now seem to have
come full circle. Some hepatologists recommend TIPS
(transjugular intrahepatic portosystemic shunt), an inter-
ventional radiologic form of side-to-side portocaval anas-
tomosis that relieves sinusoidal portal hypertension, for
the treatment of refractory ascites in carefully selected
patients,23 but this has yet to be supported by results of
ongoing randomized trials. Several other variations on the
theme of ascites recycling held the stage for a while, rang-
ing from simple intravenous infusion of the drained au-
tologous ascites to the use of an apparatus that removes,
ultrafilters and concentrates the ascites before returning it
to the patient intravenously.24 The introduction in 1974
of surgical peritoneovenous shunting by LeVeen et al. was hailed as a panacea for a couple of decades, but this too has largely been discarded because of poor long-term shunt patency, excessive complications and, because it offers no survival advantage to the patient. Parenthetically, at the Medical University of South Carolina, where the late Harry LeVeen practised for many years, we continue to have success with this procedure (probably because of the presence of Harry’s indomitable spirit) in selected end-stage liver disease patients for whom there are no other options, as well as in carefully chosen transplantation candidates, and a few recipients who have refractory but transient posttransplantation ascites.

Thus in the last quarter of the 20th century, there was a clear and present need to reappraise the safety and feasibility of large-volume paracentesis and to challenge the dogma concerning its dangers. In prospective studies on cirrhotic patients with tense ascites, with or without peripheral edema, single large-volume (5 L) paracentesis did not compromise plasma volume or renal function. However, the landmark article, whose gravitational pull was responsible for the current tidal wave of large-volume paracentesis worldwide, was published from Barcelona in 1987. In that article, Ginés et al. reported on a prospective randomized trial that compared repeated large-volume (5 L) paracentesis with albumin infusion to standard diuretic therapy in the treatment of cirrhotic patients with tense ascites (without severe liver failure or renal failure). The results showed that repeated large-volume paracentesis was one third more effective in eliminating ascites and three times quicker than standard diuretic therapy, with fewer complications (like electrolyte derangement and encephalopathy). Subsequently, investigators from the same unit in Barcelona showed that rapid total volume paracentesis using a high capacity suction pump and albumin infusion is equally safe and efficient (see Figure). What is still unclear is whether total-volume paracentesis should be used as initial therapy in any patient with large or tense ascites or must be reserved only for patients with refractory ascites. More controversial still is whether albumin replacement following the removal of more than 5 L of ascitic fluid, is truly necessary. Those in favor of albumin argue that it avoids paracentesis-induced circulatory dysfunction (characterized by activation of the renin-angiotensin-aldosterone system) that, in turn, may be associated with rapid reaccumulation of ascites, hepatorenal syndrome, dilutional hyponatremia, increased portal pressure, and shortened survival. Opponents argue that there is no measurable difference in outcome due to albumin use.

Unlike other problems of the 20th century, two of the three controversies over ascites have been resolved. In the point-counterpoint debates over overflow versus underfill, unanimity has been restored with the peripheral arterial vasodilatation hypothesis, and for the treatment of refractory ascites, total volume paracentesis now rules. It should not be long before we know whether the administration of albumin following large-volume paracentesis is simply a costly cosmetic or, as some now suspect, a “new” therapeutic balm?

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References