Fig. 3. Myelograph shows spinal cord compression related to luxation of spine.

hemothorax. This was enough to restore efficient cardiac activity. Extracorporeal circulation was started. The left pleura was then opened and several liters of blood were sucked out. The aortic isthmus was totally ruptured. The repair necessitated the placement of a Dacron graft. This patient is now leading a normal life at 5 years of follow-up.

CASE 3. In July 1990, a 28-year-old man was admitted to our department after a motor vehicle accident. On clinical examination, the patient was found to be paraplegic. The chest radiograph showed a mediastinal enlargement and a fracture of the sixth thoracic vertebra. Aortography revealed a transection of the mid descending aorta. Because of the spinal lesion, the patient was operated on in a rigid shell, which made thoracotomy impossible. A sternotomy was performed with cardiopulmonary bypass. At the level of rupture, the dorsal aspect of the aorta was incarcerated between the luxated vertebral bodies of the sixth and the seventh thoracic vertebrae. The aorta was repaired with a Dacron graft. Postoperative myelography showed a spinal cord compression related to the luxation of the spine (Fig. 3). The patient recovered totally from his paraplegia and was discharged 75 days later. Sixteen months after his accident, the patient is living a normal life.

Recent reports on traumatic rupture of the thoracic aorta have emphasized the high mortality rate related to the severity of the associated injuries.¹ In case of massive hemorrhage from the left hemothorax, emergency thoracotomy appears to be

unsuccessful.² We therefore believe that median sternotomy may sometimes be more effective.

In case 1, we preferred sternotomy because of the possible involvement of the aortic arch and the unstable fracture of the pelvis. In case 2, the patient was in cardiac arrest. Median sternotomy can be more easily and promptly performed during cardiac resuscitation than a left thoracotomy. Pericardiotomy first, in cases of cardiac arrest caused by massive and compressive left-sided hemothorax, immediately restores an efficient cardiac function and avoids the risk of complete exsanguination from pleurotomy first. In case 3, the patient was already paraplegic. The spinal injuries, especially those accompanied by neurologic deficit, may not physically tolerate a lateral decubitus position, which can increase the spinal cord compression. Sternotomy allowed us to operate with the patient in a dorsal position within a rigid shell. The cardiopulmonary bypass with a sustained spinal cord perfusion avoided adding the effects of ischemic to those of the traumatic spinal cord injuries.^{3,4} This patient recovered totally from his paraplegia.

Obviously, the exposure of the descending thoracic aorta is better through a left thoracotomy than through a median sternotomy. Use of the median sternotomy approach should be rare. However, we believe that it is an alternative in the most severe cases of acute traumatic rupture of the descending thoracic aorta: total rupture of the aorta, associated unstable spinal or pelvic fracture, and associated injuries of the transverse arch.

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REFERENCES

1. Kirklin JW, Barratt-Boyes BG. Acute traumatic transection. In: Kirklin JW, Barrett-Boyes BG, eds. *Cardiac surgery: morphology, diagnostic criteria, natural history, techniques, and indications*. New York: Wiley, 1986.
2. Cowley RA, Turney SZ, Hankins JR, Rodriguez R, Attar S, Shankar BS. Rupture of thoracic aorta caused by blunt trauma: a fifteen-year experience. *J THORAC CARDIOVASC SURG* 1990;100:652-61.
3. Rabinsky I, Sidhu GS, Wagner RB. Mid descending aortic traumatic aneurysms. *Ann Thorac Surg* 1990;50:155-60.
4. Katz NM, Blackstone EH, Kirklin JW, Karp RB. Incremental risk factors for spinal cord injury following operation for acute traumatic aortic transection. *J THORAC CARDIOVASC SURG* 1981;81:669-74.

Extension of tissue survival time in multiorgan block preparation with a delta opioid DADLE ([D-Ala², D-Leu⁵]-enkephalin)

To the Editor:

In 1988, we¹ reported our results with a newly developed, autoperfused, multiorgan block preparation for long-term organ

Fig. 1. Distribution of organ survival time.

preservation for transplantation. When plasma from hibernating woodchucks, containing hibernation-induction trigger (HIT), was used in the preparation, the preservation time was substantially extended.² We have also previously shown that only DADLE ([D-Ala², D-Leu⁵]-enkephalin), a delta class of opioid, could induce hibernation in summer-active ground squirrels (the traditional seasonally restrictive bioassay) in a fashion similar to injection with plasma fractions derived, from deeply hibernating woodchucks, containing the HIT molecule.³ Representative mu opioids morphine and morphiceptin, as well as kappa opioids dynorphin A and U-69593, were without effect.⁴ We have also previously shown that the HIT fraction infused intracerebroventricularly into primates produced a profound yet reversible behavioral and physiologic depression (bradycardia, hypothermia, and long-term hypophagia), a hibernation-like state that could be totally reversed or blocked by the infusion of the opiate antagonists naloxone and naltrexone.⁵ Such evidence indicates the opioid nature of the HIT molecule. Only the delta class of opioids, represented by DADLE, may be intimately involved in natural hibernation. To test the hypothesis that the delta opioid DADLE could also extend tissue survival time in a multiorgan preservation experiment, we performed another group of preservation studies in which the results were comparable to those obtained from the HIT study.

Six mongrel dogs weighing 15 to 25 kg were used: 25 mg DADLE (Peninsula Laboratories, Belmont, Calif.) was given intravenously 2 hours before the operation. The surgical procedure, monitoring, and interventions during the preservation period were performed in the same manner as in the HIT study, except that DADLE (1 mg/kg every 2 hours) was substituted for HIT-containing plasma. The survival time ranged from 41 to 60 hours, with a mean of 46.6 hours (Fig. 1). Aortic systolic pressure ranged from 62 ± 6 mm Hg to 79 ± 3 mm Hg, and aortic diastolic pressure ranged from 33 ± 4 mm Hg to 49 ± 7 mm Hg. Pressures were easily adjusted by blood or plasma transfusions and no inotropic drugs were needed. Heart rate ranged from 86 ± 8 beats/min to 100 ± 12 beats/min. Left

ventricular maximum rate of pressure rise ranged from 1250 ± 323 mm Hg/sec to 1920 ± 164 mm Hg/sec. Left ventricular maximum ratio of pressure development to pressure ranged from 17.2 ± 2.2 sec⁻¹ to 25.6 ± 5.3 sec⁻¹. The serum potassium level was kept relatively low and no preparation was influenced by hyperkalemia. In all preparations, the pericardium remained intact and there was no pericardial effusion at the end of the preservation period.

Serum lactic acid level was 3.6 ± 0.4 mmol/L before the operation and increased to 7.8 ± 0.6 mmol/L at 40 hours, but the variability was large and the increase was not statistically significant. Lactate dehydrogenase isoenzyme 1, an indicator of acute myocardial infarction, was 15.98% ± 1.78% before the operation. It increased to 28.87% ± 4.17% at 44 hours, but the change was also not statistically significant. Myocardial tissue wet/dry weight ratio was 4.58 ± 0.18 after preservation, versus 4.55 ± 0.97 for normal control preparations (no statistical difference). When a gas mixture of 50% oxygen, 3% carbon dioxide, and 47% nitrogen was used, arterial blood pH ranged from 7.29 to 7.54. Arterial oxygen tension was 264 ± 32 mm Hg before the operation. During the preservation period, arterial oxygen tension was maintained between 292 ± 18 mm Hg and 348 ± 9 mm Hg; it was 324 ± 67 mm Hg at 44 hours. Arterial carbon dioxide tension was 23.8 ± 6.2 mm Hg before the operation. It ranged from 13.3 ± 3.8 mm Hg to 18.4 ± 1.6 mm Hg during the preservation period (Fig. 2). Serum lactate dehydrogenase isoenzyme 3, used for diagnosis of pulmonary emboli, decreased from 20.9% ± 2.3% before the operation to 9.8% ± 0.3% at 44 hours (*p* < 0.005). The lungs maintained good function and appearance for approximately 36 hours. Lung tissue wet/dry weight ratio was 5.70 ± 0.23 after preservation, versus 4.85 ± 0.01 for normal control preparations (*p* < 0.01). Total bile production ranged from 150 to 300 ml, with an average hourly bile output of 4.4 ml. Serum alanine aminotransferase activity was 78 ± 42 U/L before the operation. It increased to 198 ± 35 U/L at 4 hours (*p* < 0.05) then decreased gradually to 97 ± 32 U/L at 16 hours, and increased again slowly to 179 ± 97 U/L at 44 hours. Serum alkaline

Fig. 2. Heart and lung function studies during the preservation period. AOP, Aortic pressure; AOSP, aortic systolic pressure; AODP, aortic diastolic pressure; paO_2 : arterial oxygen tension; $paCO_2$, arterial carbon dioxide tension; $dp/dt/p$, left ventricular maximum ratio of pressure development to pressure.

phosphatase activity was 69 ± 17 U/L before the operation. It ranged from 53 ± 8 U/L to 105 ± 43 U/L during the preservation period. Lactate dehydrogenase isoenzyme 5, used for diagnosis of hepatic congestion or injury, changed from $36\% \pm 4.5\%$ before the operation to $27.9\% \pm 6.4\%$ at 44 hours. The effect of DADLE on liver preservation was dramatic. Normally, congestion develops quickly in dog livers during this operative procedure because of hepatic vein spasm. Liver congestion starts early, in association with opening the abdomen, and deteriorates during preservation. In this study, however, liver congestion was minimal or absent during the operation. When liver congestion occurred during the preservation period, an intravenous injection of DADLE eliminated congestion and restored normal function. Liver tissue wet/dry ratio was 3.65 ± 0.10 after preservation, versus 3.64 ± 0.81 for normal control preparations. Serum amylase activity ranged from 1049 ± 404 U/L to 1241 ± 695 U/L during the preservation period, indicating no major change in this variable. Urinary output ranged from 1600 ml to 2700 ml, with hourly urine production of 50 ± 5 ml, and there were no cases of premature renal failure. Both blood urea nitrogen and creatinine levels decreased during the preservation period. Blood urea nitrogen was 14 ± 1 mg/dl before the operation. It decreased to 6 ± 2 mg/dl at 12 hours ($p < 0.025$), and was 6 ± 1 mg/dl at 44 hours. Serum creatinine level was 1.0 ± 0.2 mg/dl before the operation. It decreased to 0.4 ± 0.1 mg/dl at 4 hours ($p < 0.01$), varied between 0.4 ± 0.1 mg/dl and 0.8 ± 0.2 mg/dl during the preservation period and was 0.7 ± 0.3 mg/dl at 44 hours. Serum potassium levels varied between 1.9 ± 0.2 mmol/L and 2.9 ± 0.5 mmol/L and total calcium levels varied between 8.0 ± 0.7 mg/dl and 9.9 ± 1.6 mg/dl during the preservation period. Serum sodium and chloride levels remained at normal values during the entire experiment. The hematocrit value was stable and the white blood cell count decreased substantially during the preservation period. Free plasma hemoglobin did not increase significantly.

These results indicate that DADLE can effectively extend tissue survival time in much the same way as HIT in this preparation. This study also produced one of the longest average survival times for organ preservation. Studies of the binding of opioid drugs and peptides to specific sites in brain and other organs have suggested the existence of perhaps as many as eight types of opioid receptors. DADLE belongs to a family of morphine-like opioid agonist substances. It acts as an agonist primarily at μ , κ , and δ receptors.⁶ Therapeutic doses of morphine-like opioids produce peripheral vasodilation, reduced peripheral vascular resistance, and an inhibition of baroreceptor reflexes. The peripheral arteriolar and venous dilation produced by morphine involves several mechanisms. Morphine and most opioids provoke the release of histamine, which sometimes plays a role in the hypotensive response. A similar effect was seen in our study. When DADLE was given to anesthetized animals, systemic blood pressure decreased to as much as 50% of the original value. The reduction in liver congestion was probably related to the ability of DADLE to antagonize hepatic vein spasm, which resulted in the elimination of hepatic congestion. However, the overall effect of DADLE in our multiorgan preservation system extended beyond vasodilation. The improvement of heart and lung function, the elimination of renal failure, and the extension of survival time all seem to suggest a more extensive effect of DADLE.

To track the metabolism of DADLE, we studied the multi-organ preparation with a radionuclide technique. DADLE labeled with iodine 125 (7.5 mg) was injected into the inferior vena cava and the organ system was imaged with a γ camera (Siemens Medical Corp., Iselin, N.J.). The liver, followed by the heart a short time later, had the highest local concentrations of DADLE. Two hours later, most of the DADLE was secreted primarily in the bile and secondarily in the urine, with only a small trace of radiolabeled DADLE seen in the heart and liver. Surprisingly, the lungs did not accumulate any of the labeled DADLE during the procedure, whereas the extension of the

lung tissue preservation time was impressive. The mechanism by which DADLE contributes to tissue survival time may be similar to that of HIT. That is, it may be related to the following factors: (1) the inhibition of tissue metabolism, (2) the effect of reducing or eliminating liver congestion, and (3) a reduction in hemolysis. The beneficial effect of DADLE in organ preservation has never been reported before. Whether DADLE mediates these effects through opioid receptors is presently not known.

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REFERENCES

1. Chien S, Todd EP, Diana JN, O'Connor WN. A simple technique for multiorgan preservation. *J THORAC CARDIOVASC SURG* 1988;95:55-61.
2. Chien S, Oeltgen PR, Diana JN, Shi X, Nilekani SP, Salley R. Two-day preservation of major organs with autoperfusion and hibernation induction trigger. *J THORAC CARDIOVASC SURG* 1991;102:224-34.
3. Oeltgen PR, Nilekani SP, Nuchols PA, Spurrier WA, Su TP. Further studies on opioids and hibernation: delta opioid receptor ligand selectively induced hibernation in summer-active ground squirrels. *Life Sci* 1988;43:1565-74.
4. Oeltgen PR, Welborn JR, Nuchols PA, Spurrier WA, Bruce DS, Su TP. Opioids and hibernation. II. Effects of kappa opioid U69593 on induction of hibernation in summer-active ground squirrels by "hibernation induction trigger" (HIT). *Life Sci* 1987;41:2115-20.
5. Oeltgen PR, Walsh JW, Hamann SR, Randall DC, Spurrier WA, Myers RD. Hibernation "trigger" opioid-like inhibitory action on brain function of the monkey. *Pharmacol Biochem Behav* 1982;17:1271-4.
6. Höllt V. Opioid peptide processing and receptor selectivity. *Ann Rev Pharmacol Toxicol* 1986;26:59-78.

Antegrade aortic balloon dilatation through an apical ventriculotomy under echocardiographic control

To the Editor:

We report the use of antegrade balloon aortic valvotomy through an apical ventriculotomy under echocardiographic control in an extremely small infant. The management of critical aortic stenosis in small infants remains difficult. With percutaneous femoral aortic balloon valvotomy, the femoral artery may be damaged^{1,2} or problems may be incurred related to manipulation of the catheter around the aortic arch³ and across

the aortic valve. Operations with either bypass or blind Hegar dilatation also carry special problems in small infants.

Aortic stenosis was diagnosed on day 1 in a 32-week gestational age, 1.52 kg male infant. Echocardiography demonstrated a peak instantaneous aortic valve pressure gradient of 70 mm Hg, normal left ventricular function, and a large persistent ductus arteriosus. There was no clinical or radiologic evidence of cardiac compromise. The persistent ductus arteriosus closed by day 4 without ill effect. On day 19 tachypnea and cardiomegaly developed. Echocardiography revealed left ventricular dysfunction (shortening fraction 20%), with peak instantaneous aortic valve gradient unchanged (75 mm Hg). Because of the infant's size, percutaneous retrograde balloon dilatation was considered inadvisable. We therefore performed an apical transventricular antegrade balloon aortic valvotomy. This was performed through a 3 cm anterolateral thoracotomy through the fifth left intercostal space with the patient in the right decubitus position. After placement of a pledget-supported ventriculotomy pursestring suture, a 4.5 mm (diameter) × 3 cm (length) balloon catheter was advanced across the aortic valve with the introducing stylet in situ. Two-dimensional echocardiography was used to guide the catheter tip by means of parasternal long-axis views from the upper right sternal edge and midsternum. This allowed good visualization of the balloon catheter without interfering with the operative field. The balloon was inflated twice while across the aortic valve. The procedure was complicated by ventricular fibrillation and blood loss from the ventriculotomy. Ventricular fibrillation occurred as the catheter transiently abutted the ventricular septum, but sinus rhythm was restored with internal direct-current shock (5 J). Bleeding was caused by extension of the ventriculotomy. The balloon, despite being adequately positioned across the aortic valve, still protruded slightly from the insertion site, extending the ventriculotomy and its pursestring suture at inflation. The bleeding was controlled with a second pursestring suture. After valvotomy, the peak instantaneous aortic valve gradient was reduced to 25 mm Hg, with improved aortic valve opening and left ventricular function and only mild aortic incompetence. The postoperative recovery was complicated by coagulopathy, which resolved rapidly, and the infant was extubated 4 days after valvotomy (day 24). Six months after valvotomy, the patient's neurologic status, feeding, and growth were normal. Echocardiography revealed a peak instantaneous aortic valve gradient of 85 mm Hg, normal left ventricular function, mild aortic incompetence, but increasing left ventricular posterior wall thickness. A retrograde transarterial balloon dilatation was subsequently performed in the cardiac catheterization laboratory, successfully reducing the aortic valve gradient to 35 mm Hg.

Antegrade balloon aortic valvotomy under echocardiographic control through a limited anterolateral thoracotomy is a viable therapeutic alternative in extremely small infants with critical aortic stenosis and in those patients for whom conventional surgical valvotomy presents a high risk. Balloon valvuloplasty theoretically results in more uniform valve disruption than does a Hegar dilator, which applies force linearly to the valve.³ Access through a limited anterolateral thoracotomy allows adequate exposure of the left ventricular apex and from there a direct line to the aperture of the doming aortic valve, avoiding the need for bypass. This approach allows use of two-dimensional echocardiography to guide balloon position from the upper right sternal edge without impinging on the sterile field.