MANAGEMENT OF MAJOR HEPATIC RESECTION IN INFANTS AND CHILDREN REPORT OF SIXTEEN CASES

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EXTENSIVE HEPATECTOMY has always been a challenge to both the surgeon and the anaesthetist. Even today, peroperative and post-operative mortality is as high as 30 per cent to 40 per cent.⁵⁻⁷ Although the surgical techniques have been greatly improved by Quattlebaum,¹ Pack,² McDermott,³ Longmire⁴ and others, the operative complications remain numerous. Sudden, massive and uncontrollable haemorrhage^{5,6,8,9} is the most serious of these and sometimes is fatal. As the blood volume of the neonate, the infant and the child is small, blood loss may easily be under-rated or over-estimated; in either case, the consequences could be serious.

At Ste. Justine Hospital for children in Montreal (S.J.H.M.) 16 patients had major hepatic resections between 1965 and 1972. These cases will be presented. Preoperative evaluation and operative management will be reviewed and some of the early post-operative complications will be summarized.

In our series there were seven females and nine males. Their ages ranged from 14 days to 13 years and their weight from 2.3 to 48 kg. Their expected blood volumes varied from 184 ml to 3840 ml, based on an average of 80 ml/kg of body weight for all age groups.

There were eleven cases of hepatic tumour and five post-traumatic hepatic lacerations. Twelve had resection of the right hepatic lobe, and four of the left.

The anaesthetic agents were halothane in ten cases, droperidol or narcotics in four cases, methoxyflurane in one case and oxygen only in one patient who was comatose.

Moderate hypothermia (between 29° C and 33° C) was used during operation on nine occasions. The average age in this group was 3 years and 10 months and the average operating time was 7 hours and 30 minutes.

The other seven patients were operated upon without hypothermia; their average age was 7 years and 3 months, and the average operating time was 4 hours and 25 minutes.

RESULTS

1. *Mortality*: Four of the sixteen patients died, for an average mortality of 25 per cent. Brief details of these cases follow.

(a) J.C. (77-24-00) a seven-year-old – weighing 25 kg – brought to the opera-

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TABLE I

<i>Indication for Hepatic Resection</i>		Total	Death	% Mortality
A. Hepatic tumour		11	1	9
Hepatoblastoma (2)				
Hepatocarcinoma (3)				
Haemangioma (2)				
Metastatic (3)				
(Wilms tumour)				
Rhabdomyosarcoma (1)				
B. Hepatic trauma		5	3	60
<i>Extent of Liver Resection</i>				
	Trauma	Tumour	Death	% Mortality
Right lobectomy (12)	5	7	4	33
Left lobectomy (4)	0	4	0	0
<i>Influence of hypothermia</i>				
	Trauma	Tumour	Death	% Mortality
Hypothermia (9)	2	7	1	11
without Hypothermia (7)	3	4	3	43

ting room in shock from multiple trauma. An exploratory laparotomy was done and an attempt was made to resect the right hepatic lobe. The patient received 10,000 ml of blood, representing five times his blood volume. Death was confirmed 1.45 hours after the beginning of the operation. At the autopsy, a laceration of the right pulmonary hilum with haemothorax and laceration of the kidneys accompanied by retro-peritoneal haemorrhage were found as well as a fracture of the right femur.

(b) C.C. (68-18-34) a 3-year-old with multiple trauma, weighing 13 kg, had right hepatectomy and splenectomy. He received 3,500 ml of blood representing 3.3 times his blood volume. Following two cardiac arrests, it was noted that his blood coagulability was unsatisfactory and he died 30 minutes after the end of the operation. At the autopsy, fractures of the right femur and the fifth right rib were also noted.

(c) A.D. (60-25-41), a 10-year-old weighing 30 kg was operated on for hepatic laceration following a fall. Liver haemostasis was achieved with suture and packing. Twenty days later, he was reoperated for hepatic haematoma which was incised and drained.

Twenty-seven days after the last operation, gastrointestinal haemorrhages occurred and a negative exploratory laparotomy was followed by a gastrostomy. Two days later, the child was still bleeding from the gastrointestinal tract and was found to have haemobilia. A right hepatectomy was carried out. During dissection of the hepatic veins massive bleeding occurred and the child died on the table. He had received 6,000 ml of blood or about 2.5 times his blood volume.

(d) M.L. (65-84-77), a 15-month-old child weighing 12 kg with a malignant hepatoma underwent a right hepatectomy under hypothermia of 88° F. He had three cardiac arrests and died on the table after 8 hours and 50 minutes of operation. He received 900 ml of blood, about equal to his blood volume.

Of the four deaths, only one patient was under hypothermia. Three deaths occurred in patients with trauma and one in a patient with a malignancy.

2. *Blood Loss:* Average blood loss during the operation was about 2.2 times the estimated blood volume.

The average loss for a left hepatic lobectomy was 1.4 times the estimated blood volume and for a right lobectomy about 2.5 times. For a traumatic hepatic rupture, average loss was 3.5 times the estimated blood volume and for a hepatic tumour it was about 1.7 times.

There was no difference between the losses under normothermia and hypothermia. In both cases the average blood losses were 2.2 times the estimated blood volume.

3. In our series we had two cases of haemobilia, one of whom survived.⁴² Two of the five trauma cases were under hypothermia and survived (40 per cent survival).

Only one of the nine patients operated upon under hypothermia died (89 per cent survival). Three of the seven patients who were not under hypothermia died (43 per cent mortality).

PREOPERATIVE EVALUATION

(a) A *history* and *physical examination* are essential but may be difficult to obtain in newborns and infants.

(b) Usually *hepatic function*⁸ (as measured by transaminase, lactic dehydrogenase, alkaline phosphatase, serum electrophoresis, prothrombin time etc.) was not altered significantly. However, liver function studies served as a baseline for evaluation of hepatic function after resection. The measurement of catecholamines and cystothionine in the urine is of more diagnostic value in the evaluation of a mass in the liver of a child. Urinary catecholamines, and especially vanilylmandelic acid (VMA) are often elevated in cases of neuroblastoma, which is a common metastatic liver tumour in children.¹⁰⁻¹¹ Cystothionuria has been found in children with hepatoblastoma.¹²

(c) *Liver Biopsy*: In elective cases liver biopsy provides an accurate diagnosis.

(d) *Radiologic studies* (pulmonary, bones, pyelography, cholangiography, etc.) are important in the preoperative evaluation. More precise evaluation may be obtained with the following procedures:

- (i) Radioactive liver scanning, which may reveal the presence, site and extent of the hepatic lesion.
- (ii) Inferior vena cavography and if possible supra-hepatic venography:
 - (a) In the case of tumours, the cavography may reveal inferior vena caval occlusion, which may be due to compression or invasion.
 - (b) In trauma patients, these investigations may show involvement of the supra-hepatic veins and/or the inferior vena cava (e.g. laceration or rupture).
- (iii) Abdominal aortography^{14,15,20} is invaluable in revealing, localizing, and delineating the lesion and its blood supply.

OPERATIVE MANAGEMENT AND COMPLICATIONS

- A. *Preparations for the operation* are of such importance that they may mean the difference between success and failure. Equipment and material which must be in readiness comprise:

TABLE II
SURVEY OF FIFTEEN PATIENTS

Patients	Sex	Age	Weight (kg)	Operation	Operating Time (hr)	Hypothermia	*Blood Volume (ml)	Blood Loss (ml)	B.L. % B.V.	Diagnosis	Result	Others
M.V. 69-47-18	♀	4 years	15	Partial right lobectomy	3.30	—	1,200	500	42	Metastatic Wilms tumour	O.K.	
M.Y. 66-76-24	♂	7 years	26	Left lobectomy	3.20	—	2,080	900	43	Metastatic Wilms tumour	O.K.	
J.C. 77-24-00	♂	7 years	25	Right lobectomy	1.45	—	2,000	10,000	500	Trauma	Death	
C.C. 68-18-34	♀	3 years	13	Right lobectomy	5	—	1,040	3,500	330	Trauma	Death	coagulation problems
A.D. 60-25-41	♂	10 years	30	Right lobectomy	4	—	2,400	6,000	250	Trauma	Death	haemobilia
M.O. 41-37-10	♂	13 years	48	Left lobectomy	5.15	—	3,840	1,650	43	Hepatocar- cinoma	O.K.	
S.D. 72-42-77	♂	7 years	22	Right lobectomy	8.15	—	1,760	6,500	370	Rhabdomyo- sarcoma	O.K.	
N.B. 72-89-00	♀	5 years	22	Partial right lobectomy	5.40	88° F	1,760	550	32	Metastatic Wilms tumour	O.K.	

TABLE II (concluded)

Patients	Sex	Age	Weight (kg)	Operation	Operating Time (hr)	Hypothermia	*Blood Volume (ml)	Blood Loss (ml)	B.L. % B.V.	Diagnosis	Result	Others
M.L. 65-84-77	♂	15 months	11	Right lobectomy	8.50	88° F	880	900	100	Hepatocarcinoma	Death	
J.M. 65-25-84	♂	8 years	25	Right lobectomy	6.25	85° F	2,000	3,000	150	Trauma	O.K.	Haemobilia
D.B. 79-51-83	♀	6 years	23	Right lobectomy	10	89° F	1,840	9,250	500	Trauma	O.K.	
F.L. 71-52-70	♀	14 days	3.7	Left lobectomy	7½	92° F	300	800	270	Cavernous haemangioma	O.K.	
J.M. 77-83-38	♀	21 days	2.3	Left lobectomy	3.45	92° F	184	375	200	Haemangioma	O.K.	
D.M. 80-42-86	♀	8 months	6.4	Right lobectomy	10.40	90° F	510	1,830	360	Hepatoblastoma	O.K.	Right kidney agenesis
R.F. 76-35-56	♂	12 years	26	Extended right lobectomy	8.15	90° F	2,080	5,500	260	Hepatocarcinoma	O.K.	
A.P. 83-01-33	♂	15 months	10	Right lobectomy	7.55	88° F	800	1,300	160	Hepatoblastoma	O.K.	

*Approximate blood volume based on an average of 80 mls/kg of body weight for all age groups.

1. A tracheal tube of appropriate size which will remain *in situ* for up to 15 hours or longer.
2. A mechanical ventilator (volume cycled e.g. Engström) with humidification of inspired gases.
3. Fresh ACD blood collected the same day in large quantities (about twice the estimated blood volume) and equipment to warm the blood rapidly prior to administration.
4. A temperature controlled mattress to warm or cool the patient.
5. Arterial canula (radial) for continuous pressure monitoring and sampling for blood gases, blood sugar, haemoglobin, haematocrit, platelets, electrolytes, etc.
6. Facilities for central venous pressure monitoring (C.V.P.).
7. A second secure intravenous catheter in an upper limb for rapid blood administration (the lower limb is to be avoided because of clamping or possible laceration of the inferior vena cava).
8. Placement of a urinary catheter to avoid urinary bladder distention,⁵⁰⁻⁵² and to monitor tissue perfusion.
9. A naso-gastric tube.
10. An oesophageal stethoscope.
11. An oesophageal and/or rectal telethermometer.
12. A cardioscope.
13. A defibrillator.
14. An infra-red lamp, which is helpful if rapid rewarming is required.
15. The following drugs: isoproterenol, epinephrine, sodium bicarbonate, digitalis, 2 per cent lidocaine, epsilon aminocaproic acid, 50 per cent glucose, calcium gluconate, vitamin K, and a sufficient number of syringes and needles of all sizes.

In our series, the four deaths were associated with deficiencies in the requirements.

- B. *Anaesthetic management:* For the elective cases, meperidine (1 mg/kg) and atropine (0.01 mg/kg) are given intramuscularly one hour before the operation.

The induction is started with intravenous administration of sodium thiopentone (3 to 5 mg/kg); succinylcholine chloride (1 mg/kg) is ordinarily given to facilitate the intubation.

For maintenance of anaesthesia, we believe that halothane is a satisfactory agent for this kind of operation, even though some authors have stressed that the use of this agent cannot be recommended in conditions associated with hepatic involvement.¹⁶⁻¹⁷⁻¹⁸ Halothane has some well known advantages. One of these is the peripheral vasodilatation which assists in the induction of hypothermia. Another is that halothane is largely and rapidly eliminated when its administration is stopped, which can be of help in cardiac arrest. For elective cases where haemorrhage is usually less dramatic we prefer intravenous agents such as Innovar.

Gallamine is excreted unchanged in the urine, and is recommended as the muscle relaxant for these patients.

- C. *Hypothermia:*¹⁹ In spite of the increased hazard of myocardial irritability in

infants, with consequent ventricular fibrillation, hypothermia may be beneficial in reducing the metabolic rate and thus providing some protection to the liver. Ischaemia of the remaining liver tissue may occur because of manipulation, stasis and kinking of the hepatic pedicle or of the inferior vena cava. Moreover, hypothermia will allow a longer clamping time of the hepatic pedicle if that should become necessary.^{21,22} It also affords some protection to hepatic and cerebral cells in the event of circulatory failure.^{23,25,30} Of our nine hypothermia cases, one died, and many of the survivors had cardiac arrests varying from 30 seconds to 30 minutes. None had neurological or other sequelae. Hypothermia also diminishes the concentrations of anaesthetic agents required, beneficial since the majority (both inhalational and intravenous) are detoxified by or have noxious effects on the liver.

In view of the disturbed hepatic glycogenolysis, hypothermia protects against the neurological sequelae of hypoglycaemia by reducing cellular metabolism and the liberation of insulin. Usually a 5 per cent glucose infusion will maintain a serum blood sugar level of 200 mg or more, depending on the rate of administration.

In the light of these nine cases and others, we conclude that generally infants and children tolerate temperatures below 30° C poorly. At temperatures of less than 30° C any insult, such as sudden haemorrhage, could precipitate a cardiac arrhythmia or even fibrillation. Therefore it is preferable to avoid temperatures below 30° C.

- D. *Massive Haemorrhage*: Sudden, massive and uncontrollable haemorrhage constitutes one of the most fearsome and sometimes fatal complications.^{6,9,27} It usually occurs when dissection is being carried out around the hepatic veins near the inferior vena cava. The child may lose twice his blood volume. Enough fresh ACD blood warmed to body temperature before administration¹³ should be available. Children tolerate fresh warm ACD blood well. Yet it must be mentioned that some authors believe that children tolerate heparinized blood better. Considering the small blood volume of the newborn and infant it is easy to over-estimate or under-estimate blood losses, with serious outcome in either case.

Taylor⁶ notes in his series one death because the blood administration catheter was in a hepatic vein; that is, in the operative field.

During massive haemorrhage, the best indices are the C.V.P., continuous arterial pressure monitoring and the appearance of the liver; the cardioscope and the oesophageal stethoscope are good secondary monitors.

- E. *Air or tissue emboli*: Air²⁴⁻²⁶ or tissue emboli⁴¹ have caused some operative deaths. Due to the subatmospheric thoracic pressure and the velocity of blood flow, air and/or tissue may be sucked into an open vessel. Quattlebaum,¹ Pack,² McDermott³ and others recommend a thoracoabdominal incision to minimize this hazard. This approach was used in our series, especially for right hepatic lobe resection.
- F. *Hypoglycaemia*:^{3,28,29} Hypoglycaemia may supervene during operation and have serious neurological sequelae. One of the functions of the liver is to maintain normoglycaemia. Major hepatic resections impair the ability of the

liver to perform this function to a degree and for a period of time proportionate to the amount of normal parenchyma excised. Hypothermia and a 5 per cent glucose infusion are satisfactory safeguards. However, if no hypothermia is used, a 10 per cent glucose infusion would be safer. It is advisable to check blood glucose concentration at intervals, especially when clamping of the hepatic pedicle is necessary. Hyperkalaemia⁵³ and acidosis⁵⁴ occur following release of hepatic pedicle occlusion.

- G. *Blood Sequestration in the Splanchnic Bed*: Blood sequestration in the splanchnic bed following extensive hepatectomy may reach 60 per cent of the blood volume.⁷ This is due to a reduction in the number of vessels draining the liver and the portal bed. Following a minor resection the alterations are minimal. However, with a larger resection, all the splanchnic area will have to drain through the remaining hepatic lobe, leading to increased pressure in the portal bed. At the same time the residual liver becomes passively engorged. To prevent peripheral hypovolaemic shock, additional volumes of blood or some other colloid must be administered. The central venous pressure is the only accurate guide since blood volume determinations are seldom reliable under these circumstances.

This relative hepatic venous obstruction may persist for several days while a gradual dilatation of the residual hepatic veins takes place.

- H. *Coagulation Problems*: The large quantity of ACD blood transfused and damage to liver parenchymal may cause bleeding problems. The insult to the hepatic parenchyma may activate the fibrinolytic system⁴⁷ which will exhaust fibrinogen, prothrombin, and factors V, VII, IX, and X. Epsilon-amino-caproic acid (Amicar) given intravenously and as a 1 per cent solution for irrigation of the sectioned part of the liver,³¹⁻³³ and rapid termination of the procedure may remedy the condition.

Warm fresh blood will avoid the problems of massive stored blood transfusions (acidosis, hypocalcaemia, hyperkalaemia, thrombocytopenia, hypofibrinogenaemia, reduction of 2, 3 DPG, etc.).

While calcium administration with massive blood transfusion remains controversial,³⁶⁻³⁹ it nevertheless is our policy to administer calcium gluconate, 100 mg for each 150 to 200 ml of blood given.

Blood samples for Ca^+ , K^+ , glucose, platelets, prothrombin and fibrinogen should be obtained at regular intervals.

In elective cases, we recommend the administration of vitamin K for two days prior to operation.

IMMEDIATE POST-OPERATIVE MANAGEMENT

- A. *Ventilation*: These patients are candidates for post-operative atelectasis because of the large thoraco-abdominal incision. The right side is usually involved, but Quattlebaum⁴⁰ reports a left atelectasis with death. We therefore recommend mechanical ventilation with humidified air for about 5 hours in the immediate post-operative period with periodic over-inflation of the lungs to prevent miliary atelectasis.

- B. *Rewarming* should be slow if hypothermia was used. Usually there is no shivering on rewarming but should it happen, meperidine and promethazine is the treatment of choice.
- C. *Extubation*: It is advisable to give steroids prior to extubation to minimize subglottic oedema, and to keep the patient in a high humidity atmosphere thereafter.
- D. *Central Venous Pressure*: C.V.P. is a good means of detecting splanchnic pooling⁵⁰ and haemorrhage.
- E. *Arterial blood gases*: PO_2 , PCO_2 and pH should be followed for control of acid-base balance.
- F. *Maintenance of blood sugar*: During the first few days and sometimes for longer periods the blood glucose level is unstable, with a tendency towards hypoglycaemia, requiring 10 per cent or 20 per cent glucose infusion,^{3,6,7} to maintain normoglycaemia.
- G. *Serum albumin*: Albumin production occurs only in the liver.^{7,49} After the excision of large amounts of hepatic parenchyma, there is a failure to replenish albumin losses adequately. Thus it is necessary to give albumin to prevent hypoalbuminaemia. In patients who have undergone major hepatic resection, the combination of hypoalbuminaemia and portal hypertension may produce an almost unmanageable ascites.⁷
- H. It is necessary to give vitamin K supplement and to assess urinary output and serum electrolytes.

MAJOR POST-OPERATIVE COMPLICATIONS

Major post-operative complications may be tabulated as follows:

1. Haemorrhage^{5,20} and splanchnic sequestration of blood may result in hypotension and possibly shock.
2. Pulmonary complications, atelectasis, pleural effusion, pneumonia, pneumothorax, right diaphragmatic paresis, all with consequent hypoventilation.
3. Subphrenic abscess.^{5,27,42}
4. Biliary fistula.
5. Stress ulcer.²⁷
6. Ascites.
7. Jaundice.⁴⁵
8. Hypoglycaemia.^{3,6,7}
9. Infectious mononucleosis^{43,44,D.B.*} and post-transfusion hepatitis.⁴⁶
10. Hypoalbuminaemia.⁴⁸
11. Septicaemia.⁴²
12. Organ failure: Liver-Kidney.²⁷

SUMMARY

Sixteen extensive hepatectomies were performed at Ste. Justine Hospital for Children in Montreal from 1965 to 1972. Of these, five patients presented with massive trauma and eleven with primary or secondary tumour of the liver. There

were four operative deaths (25 per cent mortality), three due to trauma and one due to a hepatic tumour.

Nine patients were operated upon under mild hypothermia (29°–33° C) with one death (11 per cent mortality). Of the seven children without hypothermia, three died (43 per cent mortality).

Blood losses averaged 2.2 times estimated blood volume in all patients, while blood losses for the trauma cases averaged 3.5 times the estimated blood volume.

*D.B. (79-51-83) had infectious mononucleosis.

Generic and Trade Names of drugs

<i>Halothane</i>	– Fluothane
<i>Meperidine</i>	– Demerol
<i>Methoxyflurane</i>	– Penthrane
<i>Lidocaine</i>	– Xylocaine
<i>Digitalis</i>	– Digoxin
<i>d-tubocurarine</i>	– Tubarine, Intocostin
<i>Gallamine</i>	– Flaxedil
<i>Epinephrine</i>	– Adrenaline
<i>Isoproterenol</i>	– Isuprel
<i>Epsilon amino caproic acid</i>	– Amicar
<i>Promethazine</i>	– Phenergan, Mapergan
<i>Droperidol</i>	– Inapsine
<i>Fentanyl</i>	– Sublimaze
<i>Droperidol</i>	– Innovar
<i>Fentanyl</i>	

RÉSUMÉ

Seize résections hépatiques extensives ont été pratiquées à l'hôpital Ste-Justine de Montréal, de 1965 à 1972. Quatre décès sont survenus durant les interventions (soit 25 pour cent de mortalité). Trois de ces décès étaient dus à des traumatismes tandis que l'autre avait pour cause une tumeur hépatique.

Neuf patients furent opérés sous hypothermie entre 29° et 33° C. De ces neuf patients, un seul est décédé (soit 11 pour cent de mortalité). Sur les sept patients qui ont été opérés sans hypothermie, il y a eu trois décès (soit 43 pour cent de mortalité). Les pertes sanguines moyennes ont été de 2.2 fois le volume sanguin apprécié des enfants; les pertes sanguines moyennes pour les traumatisés abdominaux furent de 3.5 fois leur volume sanguin apprécié.

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