tuses, and optimizing conditions for laser resection in the trachea. Preparation and cooperation by many physicians of different specialties were essential for proper care of this patient.

The authors would like to thank Dr. Jonathan Benumof for his helpful criticism of this report.

REFERENCES

1. Wong KC, Dykman PF: Anesthetic considerations for laser surgery, Surgical Application of Lasers. Edited by Dixon JA. Chicago, Year Book, 1983, pp 29–40
2. Dieter RA, Livermore J, Tu R, Pichietti J: Mucoepidermoid tracheal adenoma during pregnancy. Int Surg 68:271–272, 1983
3. Benisch BM, Abt AB, Abramson A: Granular cell myoblastoma of trachea associated with pregnancy. Chest 63:832–833, 1973
4. Millard CE: Malignant tumors of the trachea: A new outlook. Postgrad Med 55:117–119, 1974
5. Manning FA, Platt LD, Sipos L: Antepartum fetal evaluation: Development of a fetal biophysical profile. Am J Obstet Gynecol 136:787–795, 1980
6. Houston HE, Payne WS, Harrison EG Jr, Olsen AM: Primary cancers of the trachea. Arch Surg 99:132–140, 1969
7. Pearson FG, Thompson DW, Weissberg D, Simpson WJK, Kergin FG: Adenoid cystic carcinoma of the trachea. Ann Thorac Surg 18:16–29, 1974
8. Bonica JJ: Principles and Practice of Obstetric Analgesia and Anesthesia (Vol 1). Philadelphia, Davis, 1969, pp 13–39
9. Pernoll ML, Metcalfe J, Kovach PA, Wachtel R, Dunham M: Ventilation during rest and exercise in pregnancy and postpartum. Respir Physiol 25:295–310, 1975
10. Russell IF, Chambers WA: Closing volume in normal pregnancy. Br J Anaesth 53:1043–1047, 1981
11. Bevan DR, Holdcroft A, Loh L, Mac Gregor WG, O'Sullivan JC, Sykes MK: Closing volume and pregnancy. Br Med J 1:13–15, 1974
12. Fishman AP: Pulmonary Disease and Disorders. New York, McGraw-Hill, 1980, p 367
13. Roberts RB, Shirley MA: Reducing the risk of acid aspiration during cesarean section. Anesth Analg 53:859–868, 1974
14. Bonica JJ: Principles and Practice of Obstetric Analgesia and Anesthesia (Vol 1). Philadelphia, Davis, 1969, pp 673–688
15. Cohen SE, Jasson J, Talafre M-L, Chauvelot-Moachon L, Barrer G: Does metoclopramide decrease the volume of gastric contents in patients undergoing cesarean section? ANESTHESIOLOGY 61:604–607, 1984
16. Hodgkinson R, Glassenberg R, Joyce TH III, Coombs DW, Ostheimer GW, Gibbs CP: Comparison of cimetidine (Tagamet®) with antacid for safety and effectiveness in reducing gastric acidity before elective cesarean section. ANESTHESIOLOGY 59:86–90, 1983
17. Solanki DR, Suresh M, Ethridge HC: The effects of intravenous cimetidine and metoclopramide on gastric volume and pH. Anesth Analg 63:599–601, 1984
18. Katz JD, Hook R, Barash PG: Fetal heart rate monitoring in pregnant patients undergoing surgery. Am J Obstet Gynecol 125:267–269, 1976
19. Ramanathan S, Gandhi S, Arismendy J, Chalon J, Turndorf H: Oxygen transfer from mother to fetus during cesarean section under epidural anesthesia. Anesth Analg 61:576–581, 1982
20. Vourc'h G, Tannieres M, Toty L, Personne C: Anaesthetic management of tracheal surgery using the neodymium-yttrium-aluminum-garnet laser. Br J Anaesth 52:993–997, 1980
21. Sykes MK: Rebreathing circuits: A review. Br J Anaesth 40:666–674, 1968

Anesthesiology
68:631–635, 1988

Anesthesia in Familial Dysautonomia

FELICIA B. AXELROD, M.D.,* ROGER F. DONENFELD, M.D.,† FRED DANZIGER, M.D.,‡
HERMAN TURNDORF, M.D.§

Familial dysautonomia, or the Riley Day syndrome, is a rare genetic disorder affecting nervous system development.[1] Autonomic dysfunction and decreased sensation present unique problems to the anesthesiologist, and have resulted in reports of increased morbidity and mortality.[2–5]

Recent analysis of survival probability for dysautonomic patients reveals an improved prognosis.[6] Centralization of care and the development of treatment-oriented literature for physicians and patients have been significant factors. Elective surgical procedures requiring anesthesia are now performed, because risks can be reduced with appropriate anticipatory management.

Over a 16-yr period, 127 surgical procedures were performed on 81 patients with familial dysautonomia at New York University Medical Center (table 1). Regardless of the type of surgery, certain features of anesthetic care applied to all patients. The purpose of this paper is

* Professor, Department of Pediatrics.
† Fellow, Department of Anesthesiology.
‡ Associate Professor of Clinical Anesthesiology.
§ Professor and Chairman, Department of Anesthesiology.

Received from the Departments of Pediatrics and Anesthesiology, New York University Medical School, University Hospital, New York, New York. Accepted for publication November 23, 1987.

Address reprint requests to Dr. Axelrod: Department of Pediatrics, New York University Medical Center, 550 First Avenue, New York, New York 10016.

Key words: Anesthesia: pediatric. Familial dysautonomia. Sympathetic nervous system.

TABLE 1. Surgical Procedures Performed from 1970–1986: 127 Cases

Surgical	Total Number	Surgical Procedure
Abdominal surgery	58	36 fundoplication with gastrostomy 8 gastrostomies 1 gastrostomy and jejunostomy 4 fundoplication 4 exploratory laporotomy 2 cholecystectomy 1 cholecystectomy and gastrostomy 1 gastrectomy 1 esophagostomy closure
Otolaryngology	18	7 tracheostomy 6 bronchoscopy 3 adenoidectomy 1 tonsillectomy 1 rhinoplasty
Genito-urinary	13	3 cystogram and cystoscopy 5 inguinal herniorraphy 4 orchiopexy 1 femoral herniorraphy
Ophthalmology	11	3 tarsorraphy 2 cataract removal 2 capsulotomy 2 strabismus repair 1 kerectectomy 1 repair of left orbit
Orthopedics	13	3 triple arthrodesis 3 hip pin placements 3 hip pin removals 2 drainage of septic hips 1 osteotomy of toe 1 Putti-Pratt of shoulder 1 fusion of epiphyses
Neurosurgery	6	2 craniotomy (post epidural bleeds) 4 sural nerve biopsy
Obstetrics-gynecology	5	2 Cesarian section 1 cliterectomy 1 curettage 1 tubal ligation
Thoracic	2	1 lobectomy 1 rib resection
Dental	1	1 massive caries

to review our anesthetic experience in patients with familial dysautonomia, emphasizing principles of management.

MATERIALS AND METHODS

At time of writing, our Dysautonomia Treatment and Evaluation Center had 336 registered patients with familial dysautonomia. Review of records revealed that a variety of surgical procedures requiring general anesthesia were performed from 1970 through 1986. The 127 operative procedures on 81 patients are listed in table 1. The youngest patient was 9 weeks old, and the oldest patient 34 yr old.

Preoperative care focused on assuring adequate hydration and reducing apprehension. Because many dysautonomic patients have dysphagia with special difficulty in drinking fluids, chronic dehydration, and prerenal azotemia are common. In addition to chest radiograph, analysis of arterial blood gases, and complete blood count, serum electrolytes, blood urea nitrogen, and creatinine levels were determined and appropriate corrective measures taken to normalize state of hydration. Intravenous hydration for at least 12 h prior to anesthesia was routine for rehydration, as well as to avoid further fluid depletion which can occur during the preoperative NPO period.

Apprehension was frequent, and increased the likelihood of precipitating a dysautonomic crisis. The crisis is a particular manifestation of familial dysautonomia, commonly induced by stress and characterized by intractable vomiting, hypertension, tachycardia, erythematous skin blotching, and diaphoresis.[7] Diazepam (0.1–0.2 mg/kg) was administered orally the night prior to surgery, and then iv on call to the operating room. Prior to 1975, chlorpromazine was the usual premedication because it is an antiemetic, it relieves apprehension, and it lowers arterial blood pressure. Diazepam was substituted when it became the drug of choice for treatment of crisis,[8] and blood pressure responses during induction of anesthesia were noted to be less erratic. As patients have blunted responses to hypercarbia and hypoxia,[9,10] premedication with narcotics was avoided. We have used cimetadine (5 mg/kg) iv on call to reduce gastric secretions since 1979. Atropine and glycopyrolate were not given.

The prime concern of intraoperative management was stabilization of an erratic autonomic nervous system. Intraarterial lines were routinely inserted prior to induction. Pulse oximeters were added after 1985. After preoxygenation, rapid sequence induction and endotracheal intubation were accomplished with thiopental (4 mg/kg) and succinylcholine (1.5 mg/kg) using continuously applied cricoid pressure. Corneal lubrication was instilled and eyelids taped. The operating room was warmed to 21 ° C to minimize heat loss; body temperature was monitored throughout with rectal or esophageal probes.

Anesthesia was maintained with various techniques. Inhalation techniques were preferred. Fifty per cent nitrous oxide in oxygen was used with 0.5% halothane or 1% enflurane; these concentrations were increased transiently to help control brief hypertensive episodes. Starting in 1986, some patients received fentanyl-supplemented inhalation anesthesia based on the positive

experiences of Beilin *et al.*[11] For most surgical procedures, skeletal muscle relaxants were not necessary, but, in abdominal cases, succinylcholine (1 mg/kg) or pancuronium (0.08 mg/kg) were used.

Severe hypotension was defined as a systolic blood pressure decrease of 20% or more. Intraoperatively, four patients had severe hypotension accompanied by bradycardia (table 2). In one instance, there was inadequate blood replacement during gastrectomy. In the other three instances, severe hypotension was presumed to be secondary to inadequate preoperative hydration. Rapid infusion of blood and/or crystalloid (10 ml/kg) and reduction of the inhaled anesthetic concentration were effective treatments. Although vasopressors were routinely available, they were not used in any of our cases.

Ventilation was controlled throughout surgery and, periodically, arterial blood gases were analyzed. In patients weighing less than 15 kg, a humidified Mapleson-D circuit was used. In two patients undergoing fundoplication, a decrease in Pa_{O_2} intraoperatively was presumed due to atelectasis. Temporarily increasing tidal volume and FI_{O_2} effected an increase in Pa_{O_2}, which remained stable as ventilators were returned to previous settings. A nasogastric tube was passed prior to leaving the operating room routinely unless gastrostomy had been performed.

Postoperative management required careful attention to four interrelated areas: maintaining adequate ventilation, preventing vomiting and possible aspiration, controlling pain, and controlling reactive blood pressure responses. Postoperative atelectasis occurred in ten of the 58 patients who had gastrointestinal surgical procedures. The first seven of these patients were extubated in the recovery room and four (57%) developed atelectasis. The next 51 patients who had abdominal surgery remained intubated and were ventilated for 12–72 h, depending on individual requirements for pulmonary toilet and pain medication. As long as narcotics were being administered, extubation was postponed. Only six (12%) of the second group developed atelectasis. Vigorous chest physiotherapy was continued after extubation and included clapping and suctioning. Prophylactic broad spectrum antibiotics were administered routinely for 36 h. Preexisting bronchiectatic disease was considered an indication for extending antibiotic use to 5 days.

To decrease gastric secretions, cimetadine was continued postoperatively until bowel sounds were present. For patients without gastrostomies, nasogastric tubes effected stomach decompression until patients were awake and demonstrated adequate gag reflexes as protection against aspiration. Sixteen patients had dysautonomic crises in the postoperative period characterized by nausea, retching, and hypertension (table 2). Stomach decompression and diazepam iv were effective in controlling symptoms. Chlorpromazine was not used for crisis symptoms after 1975.

TABLE 2. Comparison of Anesthetic Complications

	Axelrod *et al.* (1987)	Kritchman, *et al.** (1959)
Number of anesthetics	127	27
Number of patients	81	8
Operative Complications		
Cardiac arrest	0	2 (7%)
Hypotension	4 (3%)	6 (22%)
O_2 desaturation	2 (2%)	—
Postoperative Complications		
Hypotension	1 (1%)	1 (3%)
Vomiting "crisis"	16 (13%)	3 (11%)
Pneumonia	8 (6%)	5 (18%)
Fever	6 (5%)	1 (3%)
Atelectasis	10 (8%)	—

—= complication not mentioned.
* Kritchman *et al.*[2]

Although peripheral pain sensation is diminished in familial dysautonomia, it is not totally absent. Visceral and peritoneal pain sensation is intact and can cause overt complaints and splinting. Frequently, the reaction to postoperative pain was agitation associated with hypertension and tachycardia. Occasionally the stress was sufficient to precipitate dysautonomic crisis. Patients who had orthopedic, genitourinary, obstetrical, and gynecologic procedures did not complain of postoperative pain. However, some patients did manifest agitation and crisis symptoms. For these patients, iv diazepam (0.1–0.2 mg/kg) was usually sufficient, and could be repeated at 3-h intervals. Chloral hydrate suppositories (30 mg/kg) were given to supplement the sedative effects of diazepam without producing marked respiratory depression, and could be repeated at 6-h intervals. Ophthalmologic procedures were never complicated by complaints of pain or crisis symptoms. However, patients who had abdominal surgery usually experienced considerable pain for 24–48 h, and required additional use of intermittent morphine at 0.1 mg/kg. Use of the latter drug necessitated maintaining endotracheal intubation to assure adequate ventilation.

Postoperative hypertension paralleled complaints of pain. Postoperative hypotension and decreased urine output correlated with requirements for additional fluid administration.

Hypothermia was less of a problem, as greater attention was given to maintaining intraoperative temperatures above 35° C with heated intravenous fluids and

respiratory gases, as well as warming the operating rooms. Intraoperative hyperthermia to 38.9° C occured in only one patient who had pseudomonas pneumonia documented by radiographs and tracheal aspirate cultures. Postoperative fevers were related to respiratory infections or atelectasis.

Discussion

Patients with familial dysautonomia have been considered to be grave anesthetic risks.[2] Diminished peripheral innervation results in decreased sensation and autonomic dysfunction, presenting unique management problems for the anesthesiologist. Although general anesthesia in these patients can be difficult, it is not contraindicated. Complications can be lessened or avoided if appropriate measures are taken to maintain stability of the autonomic nervous system.

The autonomic dysfunction in familial dysautonomia extends throughout multiple systems, and results in complex interrelated management problems. Cardiovascular instability pervades preoperative, intraoperative, and postoperative management. Blood pressure lability results from decreased autonomic innervation of blood vessels and organs,[1,12,13] baroreceptor insensitivity,[9] and hypersensitivity to parenteral, as well as circulating, catecholamines.[1,14] Instability is further exaggerated in the presence of decreased vascular volume or with acute oxygen desaturation.[9,10] Mean arterial pressure is the product of cardiac output and systemic vascular resistance (SVR), but, in familial dysautonomia, normal compensatory mechanisms are absent. Baseline SVR is relatively low as a result of diminished innervation of vascular smooth muscle[12] and decreased norepinephrine synthesis and release.[13,15] Cardiac output is unresponsive because of fixed inotropy and chronotropy. The combined effect makes the arterial blood pressure extremely sensitive to the vasodilatory and cardiac depressant effects of anesthetics. Consequently, cardiac output is strongly influenced by pre-load and Starling forces.

As the cardiovascular status is sensitive to a variety of factors, each with the potential to produce abrupt and dramatic changes, continuous and concurrent monitoring of multiple parameters is essential. In addition to assessment of urine output, temperature, heart rate, and breath sounds, we routinely utilized indwelling arterial catheters to monitor direct arterial blood pressures and to obtain frequent blood gases. Pulse oximetry has been an important adjunct in recent years.

Although we used thiopental for induction, no patient developed hypotension. Thiopental-induced hypotension previously reported[2] may have been due to inadequate preoperative hydration and low vascular volume. In our experience, once intravascular volume was stabilized, no appreciable intraoperative difference in autonomic stability was noted between narcotic or inhaled anesthetics. This experience generally agrees with that of Beilin *et al.*,[11] who successfully supplemented 50:50 N_2O:O_2 with fentanyl and pancuronium after benzodiazeprine induction without cardiovascular instability after paying "special attention . . . to fluid balance." Inkster[16] reported a single successful anesthetic experience with halothane, but McCaughey[5] reported severe hypotension and marked cardiovascular instability during methoxyflurane, halothane, and ether in his single patient that underwent six anesthesias. Neither Inkster or McCaughey indicated the vascular volume status of their respective patients. Four of our cases developed intraoperative hypotension. Three of the patients may not have been prehydrated adequately, and the other had a sudden intraoperative blood loss. Inhalation agents have the important advantage of rapid reversibility and titratibility to the clinical condition. We found that patients with familial dysautonomia required less than usual concentrations of inhaled anesthetics. This may be the result of decreased muscle tone and decreased pain sensation in this disorder. These patients respond normally to usual doses of succinylcholine and pancuronium. Succinylcholine has also been used by others without evidence of hyperkalemia or prolonged effect.[2,3]

As patients with familial dysautonomia have diminished sympathetic innervation, they demonstrate exaggerated responses to direct-acting sympathetic agonists and erratic responses to indirect-acting sympathomimetics. We minimized the use of autonomic drugs. Chlorpromazine premedication was discontinued. Atropine was not routinely administered because many patients have bronchiectasis, and we wished to avoid inspissated secretions. It can be used for extreme vagovagal reflexes, as no ill effects have been noted.[16,17]

Respiratory function is often compromised in patients with familial dysautonomia. Repeated aspiration predisposes to bronchiectasis.[7,8] Hypotonic musculature and spinal curvature cause restrictive lung disease. In addition, responses to hypoxia and hypercarbia are abnormal.[9,10] Endotracheal intubation must be done to control ventilation and facilitate pulmonary toilet. Pulmonary risk is greatest in the postoperative period. Vomiting and aspiration can occur. Atelectasis may result from inspissated secretions, splinting, or decreased ventilation from narcotics. We maintained endotracheal intubation and mechanical ventilation until pain and associated splinting were markedly reduced and narcotics were no longer required.

Patients with familial dysautonomia have abnormal gastrointestinal motility. Forty per cent manifest dysau-

tonomic crisis during which increased serum dopamine levels have been observed.[1] Dopamine, the medullary chemotrigger neurotransmitter, acts peripherally as an inhibitor of parasympathetic activity.[1] Diazepam, which increases GABA and may suppress dopamine release, has been effective when stress or pain precipitates a postoperative crisis. Gastric decompression and cimetadine further decrease the risk of aspiration of gastric contents.

In our experience, patients have required very little postoperative pain medication with the exception of those individuals who had gastrointestinal surgery. Diazepam and chloral hydrate generally suffice to control postoperative discomfort. In those cases where pain is more marked, judicious use of narcotics is indicated.

Conclusion

In summary, familial dysautonomia is a rare genetic disorder affecting central nervous system development. General anesthesia has been considered hazardous primarily due to autonomic instability. Our experience indicates that the special features of anesthetic care for these patients are the extra attention one must give to intravascular volume status, the frequent requirement for prolonged ventilatory support, and the use of unique antiemetic medication.

Routine hydration in the preoperative period when the patient is kept NPO corrects and prevents further dehydration. Intraoperative vascular lability is minimized also by ongoing assessment and replacement of fluid during anesthesia and careful titration of anesthetic agents to beat-to-beat variations in blood pressure and heart rate, which is facilitated by arterial line monitoring. When appropriate intravascular volumes are maintained and anesthetic agents titrated, there can be flexibility regarding choice of anesthetic agent; iv barbiturates, inhalation agents, and narcotics can be used with little risk of severe hypotension. In the postoperative period, extended intubation and ventilation may be necessary after abdominal surgery or other situations where narcotics are needed to control pain. Special precautions to minimize vomiting and aspiration are also important; diazepam is especially useful in treating dysautonomic crisis. General anesthesia presents unique problems, but should not be considered contraindicated for patients with this disorder.

References

1. Pearson J: Familial dysautonomia (a brief review). J Auton Nerv Syst 1:119–126, 1979
2. Kritchman MM, Schwartz H, Papper EM: Experiences with general anesthesia in patients with familial dysautonomia. JAMA 170:529–533, 1959
3. Meridy HW, Creighton RE: General anesthesia in eight patients with familial dysautonomia. Can Anaesth Soc J 18:563–570, 1971
4. Bartels J, Mazzia VDB: Familial dysautonomia. JAMA 212:318–319, 1970
5. McCaughey TJ: Familial dysautonomia as an anaesthetic hazard. Can Anaesth Soc J 12:558–568, 1965
6. Axelrod FB, Abularrage JJ: Familial dysautonomia: A prospective study of survival. J Pediatr 101:234–236, 1982
7. Axelrod FB, Nachtigal R, Dancis J: Familial dysautonomia: Diagnosis, pathogenesis and management, Advances in Pediatrics. Edited by Shulman I. Chicago, Year Book Publishers, 1974, pp 75–96
8. Axelrod FB: Familial dysautonomia, Current Pediatric Therapy. Edited by Gellis S, Kagan B. Philadelphia, W. B. Saunders Co., 1986, pp 92–95
9. Edelman NH, Cherniack NS, Lahiri S, Richards E, Fishman AP: The effects of abnormal sympathetic nervous function upon the ventilatory response to hypoxia. J Clin Invest 41:1153–1165, 1970
10. Filler J, Smith AA, Stone S, Dancis J: Respiratory control in familial dysautonomia. J Pediatr 66:509–516, 1965
11. Beilin B, Maayan Ch, Vatashsky E, Shulman D, Vinograd I, Aronson HB: Fentanyl anesthesia in familial dysautonomia. Anesth Analg 64:72–76, 1985
12. Grover-Johnson N, Pearson J: Deficient vascular innervation in familial dysautonomia, an explanation for vasomotor instability. Neuropath Appl Neurobiol 2:217–224, 1976
13. Ziegler MG, Lake R, Kopin IJ: Deficient sympathetic nervous responses in familial dysautonomia. NEJM 294:630–633, 1976
14. Smith AA, Dancis J: Exaggerated response to infused norepinephrine in familial dysautonomia. NEJM 270:704–707, 1964
15. Gitlow SE, Bertani LM, Wilk E, Li BL, Dziedzic S: Excretion of catecholamine metabolites by children with familial dysautonomia. Pediatrics 46:513–522, 1970
16. Inkster JS: Anesthesia for a patient suffering from familial dysautonomia (Riley-Day syndrome). Br J Anaesth 43:509–512, 1971
17. Stenquist O, Sigurdsson J: The anesthetic management of a patient with familial dysautonomia. Anesthesia 37:929–932, 1982