SERUM TRANSAMINASE LEVELS FOLLOWING PROLONGED SURGICAL ANESTHESIA

S. H. LAWRENCE, M.D., AND THOMAS SCHULKINS, M.D.

THE transamination reaction was originally described by Braunstein and Kritzman (1). The enzyme, glutamic oxalacetic transaminase, is widely distributed in animal tissues, with highest levels in cardiac muscle, skeletal muscle, brain, and liver (2, 3). La Due, Wróblewski, and Karmen (4) report elevated serum transaminase levels following myocardial necrosis and liver cell injury. Necrosis of brain tissue in cerebral thrombosis does not seem to cause a serum elevation (5). The unit of transaminase activity is defined as the amount of enzyme necessary to cause a decrease in optical density of 0.001 mμ per milliliter of serum per minute under conditions stated by Karmen (6). The level in normals varies from 8 to 40 units per milliliter and is relatively constant in any one individual from day to day (5).

This study was initiated to investigate the relationship of muscular trauma during extensive surgical procedures to the serum transaminase level. Inasmuch as electrocardiographic or clinical evidence of myocardial damage sometimes accompanies especially prolonged thoracic surgery, the relationship of this factor was also investigated.

METHODS

Twelve patients who were to undergo thoracotomy and pulmonary resection were studied. Specimens of venous blood were obtained for examination prior to operation, eight hours following it, and at daily intervals thereafter for a week. Seven patients who underwent extensive nonthoracic operations, and one who was not operated on but who was given oxygen inhalations for two hours, were used for comparison.

The blood specimens were allowed to clot, were refrigerated overnight, and the serum was separated and quickly frozen the next day. The entire series of determinations on any one patient was done at one time. The assay method of Karmen (6) was used.

RESULTS

The first 11 patients shown in table 1 are those who underwent thoracotomy and pulmonary resection. All had inhalation anesthesia with ether-cyclopropane. In each case there was an initial elevation in serum transaminase whose peak occurred between eight and forty-eight hours and then showed a gradual decline, in most cases to normal

Accepted for publication March 27, 1956. Received from the San Fernando Veterans Administration Hospital, San Fernando, California. Dr. Schulkins is Surgical Resident at the Veterans Administration Hospital, Los Angeles, California.

TABLE 1

SERUM TRANSAMINASE ACTIVITY AT VARIOUS PERIODS FOLLOWING OPERATION AND THE PERCENTAGE INCREASE IN ACTIVITY

No.	Type of Case	Hours			Days After Operation					% Peak Increase
		0	8	24	2	3	4	5	6	
*1	Carcinoma—Resection	7	40	39	27	17		8	18	470
2	TB—Resection	21		47	28		25			124
3	TB—Resection	9	18	39	17		21		16	333
4	TB—Resection	19	27	32	26		10			140
5	TB—Resection	30	49	38						70
6	TB—Resection	16	17	26	35					119
7	TB—Resection	14		36	33	36				157
8	TB—Resection	12		34	35	30	27			191
9	TB—Resection	14	23		20					70
10	TB—Resection	23	27	41	37	28				94
11	TB—Resection	10	44	54	47	57	34			470
12	TB—Resection Hepatitis	12	20	52	50	55	52		57	269
13	Lap.—Stomach	20	30	32	26	21	22			60
14	Lap.—Gall bladder	31	49		47	30	28			58
15	Lap.—Stomach	8	18		16	17	10			125
16	Lap.—Gall bladder	15	21	21	18	12				40
17	Lap.—Gall bladder	8	12	12	11	8	9			50
18	Lap.—Stomach (spinal)	10	12	14	11	10				40
19	Pericardial poudrage	22	45	70	61					218
20	Oxygen inhalation (2 hrs.)	16	15	18	16					13

* Thoracotomy repeated between fifth and sixth days.

levels within seven days. Patient no. 1, who had a second thoracotomy and resection on the fifth day, showed a secondary elevation following this operation.

Patient no. 12 developed a toxicity following thoracotomy and pulmonary resection which was accompanied by jaundice on the fourteenth day. This was assumed to be due to viral hepatitis.

Six additional patients used for comparison had abdominal operations on the stomach or gallbladder. For patients 13 through 17 inhalation anesthesia was used; patient no. 18 was given spinal anesthesia for vagotomy and partial gastric resection. The electrocardiograms were all within normal limits before and after operation and surgery was uneventful.

Patient no. 19 was a 61-year-old man who had a history of three myocardial infarctions prior to submitting to pericardial poudrage. His electrocardiogram showed extensive myocardial damage, mostly posteriorly, but no change during the preceding month.

Patient no. 20 was a convalescent whose transaminase levels were determined before and after the inhalation of pure oxygen for two hours and showed no marked change.

The following patients had cardiac complications during or following operation. Patient no. 1 underwent thoracotomy for a suspected

carcinoma of the left upper lobe. His preoperative electrocardiogram was within normal limits. During left upper lobectomy the cardiac rhythm became irregular and S–T prolongations were noted. The diagnosis of carcinoma was substantiated postoperatively and, on the seventh postoperative day, thoracotomy was repeated. During this operation the patient developed S–T and T wave changes and died, presumably from *cor pulmonale*, on the third postoperative day.

Patient no. 3 developed an arrhythmia during operation and became cyanotic. He was digitalized and the operation was completed. The postoperative course was uneventful.

Patient no. 11 developed auricular fibrillation postoperatively; this reverted to normal after the administration of quinidine and no further cardiac abnormalities were noted.

DISCUSSION

An elevation of serum transaminase occurred in all patients studied. In patient no. 20, on whom no surgical procedure was performed, the elevation (13 per cent) is considered to be insignificant. No patient on whom a major surgical procedure was performed had an elevation of less than 40 per cent. No patient who underwent thoracotomy and pulmonary resection had an elevation of serum transaminase of less than 70 per cent.

The reason for the elevation of transaminase in the serum was not at first apparent. It is believed that necrosis of transaminase-containing tissue is necessary in order that additional transaminase will be present in the serum. Thus evidence of necrosis of various transaminase-containing tissues was sought.

Heart.—Direct trauma due to surgery and manipulation in this area could occur during pulmonary resection. However, since a similar basic elevation occurred in patients undergoing abdominal surgery, trauma to the heart was eliminated as the cause of the basic elevation.

The length of the operation and the anoxemia associated with it, as well as the toxic effect of the anesthetic on the myocardium, seemed unlikely choices, especially since a basic response followed in the one case in which spinal anesthesia was employed.

Brain.—Ether and anoxia may very well affect the brain, and inasmuch as the brain tissue is an abundant source of transaminase, one would expect that necrosis of areas of the brain would be reflected in elevations in the serum transaminase levels. Such does not seem to be the case, however, in cerebral thrombosis.

Liver.—Liver damage due to the anesthetic agent might cause an elevated transaminase level, but again the basic elevation in the patient with spinal anesthesia leads us to believe that the liver damage is a transient one and cell necrosis does not occur.

Skeletal Muscle.—This seems the most likely source of the liberated transaminase responsible for the basic serum elevation. Patients with a small amount of muscle destruction showed small increases, whereas thoracotomy patients, who underwent extensive muscular dissections, showed marked elevations.

In addition to this basic elevation, 3 patients with evidences of cardiac damage and one with severe hepatitis showed extremely high levels of transaminase in the serum. The peak of the elevation in the former seemed to be within the first thirty-six hours; in the latter a gradual elevation occurred for several days.

The peak elevation seemed to occur within twenty-four hours after operation in all cases except that showing liver damage (fig. 1). In most cases the transaminase in the serum returned to normal within a week.

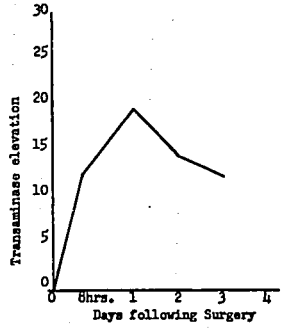

FIG. 1. Average increase of transaminase in the serum following pulmonary resection.

Whether or not a test of this nature is of any practical value in the diagnosis of cardiac damage in an isolated case showing no other evidences at the time of surgery remains to be seen. It does, however, seem to be an additional laboratory tool which might be used in selected cases.

SUMMARY

Serum transaminase levels were assayed in 19 patients prior to and at intervals following a number of surgical procedures, and in one patient prior to and following inhalation of oxygen for two hours. All patients undergoing surgery exhibited a basic increase in activity within thirty-six hours following the operation. This is interpreted to be due to skeletal muscle destruction. Four patients who had cardiac complications during operation showed more marked re-

sponses; these also occurred within thirty-six hours, and were presumably due to some myocardial necrosis. One patient developed infectious hepatitis and showed, in addition to the basic increase, a gradual one for several days. The significance and practical value of these findings is discussed.

REFERENCES

1. Braunstein, A. E., and Kirtzmann, M. G.: Über den Ab- und Aufbau von Aminosäuren durch Umaminierung, Enzymologia, 2: 129, 1937.
2. Cohen, P. P., and Hekhuis, G. L.: Rate of Transamination in Normal Tissues, J. Biol. Chem. 140: 711 (Sept.) 1941.
3. Cohen, P. P.: Transamination with Purified Enzyme Preparations (Transaminase), J. Biol. Chem. 136: 565, 1940.
4. La Due, J. S., Wróblewski, F., and Karmen, A.: Serum Glutamic Oxaloacetic Transaminase Activity in Human Transmural Myocardial Infarction, Science, 120: 497 (Sept. 24) 1954.
5. Wróblewski, F., and La Due, J. S.: Serum Glutamic Oxaloacetic Transaminase Activity as Index of Liver Cell Injury: Preliminary Report, Ann. Int. Med. 43: 345 (Aug.) 1955.
6. Karmen, A., Wróblewski, F., and La Due, J. S.: Transaminase Activity in Human Blood, J. Clin. Invest. 34: 126 (Jan.) 1955.

THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC. SEVENTH ANNUAL REFRESHER COURSE PROGRAM

SPONSORED BY COMMITTEE ON MEDICAL SCHOOLS AND POSTGRADUATE EDUCATION

Municipal Auditorium, Kansas City, Missouri

OCTOBER 8–9, 1956

LIST OF LECTURERS AND LECTURES

Course No.	*Title*	*Instructor*
M61–T611	"The Analeptics and the Treatment of Narcotic Poisoning"	John Adriani, M.D.
T13	"Chemistry in Anesthesia"	John Adriani, M.D.
M23–T23	"Practical Concepts in Pain Management"	F. A. D. Alexander, M.D.
M53–T53	"Dental Anesthesia"	Bruce M. Anderson, M.D.
M22–T22	"Ether Analgesia"	Joseph F. Artusio, M.D.
M31–T311	"Pediatric Anesthesia"	Kay Belton, M.D.
M35–T410	"Pathology of Anesthetic Complications"	Chauncey Bly, M.D.
M15	"Diagnostic and Therapeutic Nerve Block for Pain Syndromes"	John J. Bonica, M.D.
T15–T512	"Brachial Plexus Block"	John J. Bonica, M.D.
M63	"Anesthesia for Massive Excision of Organs"	C. Paul Boyan, M.D.
T63–T212	"Anesthesia for Head and Neck Surgery"	C. Paul Boyan, M.D.
M32–T32	"Neuro-Endocrine Responses during Ether Anesthesia"	William R. Brewster, M.D.
M44–T44	"Anesthesia for the Diabetic Patient during Surgery"	Seymour Brown, M.D.
M63–T55	"Anesthesia for Cardiac Catheterization Techniques"	Joseph J. Buckley, M.D.
M311–T35	"Residency Training Programs"	Donald L. Burdick, M.D.

(*Continued on page 548*)

constitutes a misuse. In such dosage ranges depression of respiration and circulation of moderate degree, a prolonged postoperative recovery, and frequently undesirable operating conditions are produced.

ACKNOWLEDGMENT

The supply of Dolitrone used in this study was furnished by the William S. Merrell Company, Cincinnati, Ohio.

REFERENCES

1. Thompson, C. R., Smith, J. K., and Werner, H. W.: Pharmacology of 5-ethyl-6-phenyl-m-thiazane-2,4-dione, Fed. Proc. 13: 411 (March) 1954.
2. Lundy, J. S.: 110 Years of Anesthesia, J.M.A. Georgia 43: 195 (March) 1954.
3. Lundy, J. S.: Will There be an Era of Analgesia? (Editorial), Journal-Lancet 74: 155 (April) 1954.
4. Lundy, J. S.: Hope for Age of Analgesia, J. Am. Nurse Anesthetists 22: 225 (Nov.) 1954.
5. Lundy, J. S.: Development of Analgesia After Century of Anesthesia, J.A.M.A. 157: 1399 (April) 1955.
6. Cotten, M. deV.: Circulatory Changes Affecting Measurement of Heart Force in Situ with Strain Gauge Arches, Am. J. Physiol. 174: 365 (Sept.) 1953.
7. Boniface, K. J., Brodie, O. J., and Walton, R. P.: Resistance Strain Gauge Arches for Direct Measurement of Heart Contractile Force in Animals, Proc. Soc. Exper. Biol. & Med. 84: 263 (Nov.) 1953.
8. Boniface, K. J., Brown, J. M., and Kronen, P. S.: Influence of Some Inhalation Anesthetic Agents on Contractile Force of Heart, J. Pharmacol. & Exper. Therap. 113: 64 (Jan.) 1955.
9. Cotten, M. deV., and Bay, E.: Comparison of Cardiovascular Properties of New Nonbarbiturate Intravenous Anesthetic Agent with Those of Thiopental, Anesthesiology 17: 103 (Jan.) 1956.
10. Kerr, M., and Kahn, J. B.: Observations on Some Newer Drugs Used for Intravenous Anesthesia with Special Reference to Dolitrone, Paper presented at Meeting of Southern Society of Anesthesiologists (April) 1955.
11. Davis, D. A., Grosskreutz, D. C., Sugioka, K., Boniface, K. J., and Tait, C. A.: Dolitrone —A New Intravenous Anesthetic: A Preliminary Report, In Press.

(*Continued from page 535*)

Course No.	*Title*	*Instructor*
M62–T61	"Cyclopropane Anesthesia"	Vincent J. Collins, M.D.
M54–T54	"Epidural (Peridural) Anesthesia"	Oral B. Crawford, M.D.
M26–T26	"Preoperative Cardiac Evaluation of the Patient for Surgery"	James E. Crockett, M.D.
M14–T14	"The Principles of Oxygen Therapy"	John B. Dillon, M.D.
M55–T11	"The Physiology of Respiration"	Robert D. Dripps, M.D.
M310–T310	"Antihistaminics and Their Role"	Paul R. Dumke, M.D.
M12–T12	"Nitrous Oxide Anesthesia"	Douglas Eastwood, M.D.
M19	"Clinical Application of Chlorpromazine to Anesthesia"	James E. Eckenhoff, M.D.
M51–T511	"Morphine and Allied Analgesics"	James E. Eckenhoff, M.D.
M42–T42	"The Use of Mechanical Resuscitators"	James O. Elam, Capt., MC
M312–T31	"Cardiac Output during General Anesthesia"	Benjamin Etsten, M.D.
M64–T64	"The Electroencephalography Applied to Anesthesia"	Albert Faulconer, M.D.
M66–T66	"Pharmacology of Curare Preparation"	Francis F. Foldes, M.D.
M27–T27	"Premedication in Anesthesia"	Harold J. Freiheit, M.D.
M56–T56	"Anesthesia for the Urological Patient"	A. William Friend, M.D.

(*Continued on page 577*)

Passive closure of the glottis, occurring in relatively deep anesthesia, may be initiated by the inspiratory flow of gas when the glottic Bernoulli effect is unopposed by abduction of the vocal cords. Further inspiratory effort may suck the vocal cords together so strongly that complete obstruction results. This probably represents a reversion to the cusp valve functioning of the vocal folds present in lower primates.

Reflex closure of the larynx is due to a ball valve mechanism consisting of the preepiglottic body and false cords, operated mainly by extrinsic muscles, notably the thyrohyoid. It may be regarded as a protective reflex response to visceral sensory stimulation, and is part of a general expiratory spasm which itself represents an extreme form of cough.

The mechanism of each type of obstruction is discussed and appropriate remedies are suggested.

REFERENCES

1. Burstein, C. L.: Fundamental Considerations in Anesthesia. New York, The Macmillan Company, 1949, p. 29.
2. Negus, V. E.: The Mechanism of the Larynx. St. Louis, C. V. Mosby Company, 1931.
3. Fink, B. R.: Mechanism of Closure of Human Larynx, Tr. Am. Acad. Ophth. 60: 117 (Jan.–Feb.) 1956.
4. Fink, B. R., Basek, M., and Epanchin, V.: Mechanism of Opening of Human Larynx, Laryngoscope, In press.
5. Curry, R.: The Mechanism of the Human Voice. New York, Longmans, Green & Co., 1940, p. 77.

(*Continued from page 548*)

Course No.	*Title*	*Instructor*
M13–T51	"Etiology, Pathogenesis and Treatment of Shock"	Donald E. Hale, M.D.
M58	"Practical Concepts in Pain Management"	Frederick P. Haugen, M.D.
M17–T17	"Physics as Applied to Anesthesia"	Mr. Wayne W. Hay
M45–T45	"Caudal-Transacral Anesthesia"	Robert A. Hingson, M.D.
M37–T37	"Anesthesia in Caesarean Section"	J. Jay Jacoby, M.D.
M48–T36	"Anesthesia for Thoracic Surgery"	John E. Keet, Capt., MC
M11–T111	"Anesthetic Management for Intracardiac Surgery, Complications and Treatment"	Kenneth Keown, M.D.
M39–T39	"An Abstract of the History of Surgical Anesthesia"	Thomas E. Keys
M33–T33	"Medico-Legal Aspects"	Mr. John Lansdale, Jr.
M18–T18	"Spinal Anesthesia"	Lloyd E. Larrick, M.D.
M46–T46	"Anesthesia for Patients with Cardiac Lesions"	Philip A. Lief, M.D.
M412–T412	"Induced Hypotension during Anesthesia"	David M. Little, Jr., M.D.
M34–T34	"Geriatric Anesthesia"	Paul H. Lorhan, M.D.
M28	"A Comparison of Intravenous Anesthesia"	John S. Lundy, M.D.
T28	"Roentgenograms in Diagnostic and Therapeutic Nerve Blocks"	John S. Lundy, M.D.
M510–T47	"Pharmacology of Barbiturates"	Lester C. Mark, M.D.
M24	"Causes and Treatment of Sudden Cardiac Collapse"	Stevens J. Martin, Ph.D., M.D.
M47–T24	"Pharmacology of Local Anesthetic Agents"	Hugh S. Matthewson, M.D.
M25	"Cervical Plexus Block"	Daniel C. Moore, M.D.

(*Continued on page 590*)

ADDENDUM

Since the completion of these experiments, there has appeared a paper by W. R. Gibson, E. E. Swanson, and W. J. Doran: Proc. Soc. Exper. Biol. & Med. 89: 292, 1955, on a short-acting barbiturate with an acetylenic linkage in one substituent group. Their compound is 1-methyl-5-allyl-5-(1-methylpentenyl) barbituric acid.

REFERENCES

1. Margolin, S., Perlman, P., Villari, F., and McGovack, T. H.: New Class of Hypnotics: Unsaturated Carbinols, Science 114: 384 (Oct. 12) 1951.
2. Stickney, J. C., Van Liere, E. J., and Northrup, D. W.: Correlation Between Propulsive Motility and Length of Small Intestine in Albino Rats and Dogs, Am. J. Physiol. 167: 399 (Nov.) 1951.
3. Hulme, N. A., and Krantz, J. C., Jr.: Anesthesia: Effect of Ethyl Ether on Oxidative-Phosphorylation in Brain, Anesthesiology 16: 627 (July) 1955.

(*Continued from page 577*)

Course No.	*Title*	*Instructor*
T25–T612	"Stellate Ganglion Block"	Daniel C. Moore, M.D.
M111–M611	"Problems of Vaporization of Ether"	Lucien E. Morris, M.D.
T–38	"Carbon Dioxide in Anesthesia"	Lucien E. Morris, M.D.
M57–T57	"The Anesthesiologist and His Role in the Treatment of Polio"	William A. O'Brien, M.D.
M511–T52	"Topical Anesthesia"	Louis R. Orkin, M.D.
M49–T–49	"The Significance of Arrhythmia to Anesthesiology"	O. Sidney Orth, M.D.
M69–T–69	"Anesthesia for Thyroid Surgery"	Robert B. Orr, M.D.
M612–Y62	"Renal Function during Anesthesia"	E. M. Papper, M.D.
M59–T59	"Cortisone Therapy and Acute Adrenal Insufficiency as Related to Anesthesia"	John W. Pender, M.D.
M512–T58	"Scientific Literature and the Anesthesiologist"	Charles B. Pittinger, M.D.
M410–T48	"Vasopressor Agents"	John K. Potter, M.D.
M210–T210	"Anesthesia for Neurosurgery"	Edwin L. Rushia, M.D.
M41	"Methods of Respiratory Resuscitation"	Max S. Sadove, M.D.
M112–T31	"Resuscitation of the Newborn"	Max S. Sadove, M.D.
M110–T110	"Anesthesia for Pelvic Delivery"	L. F. Schuhmacher, M.D.
M20–T29	"Indications and Contra-indications for Blood Transfusions, Complications and Treatment of Transfusion Reactions"	T. H. Seldon, M.D.
M38	"Problems of Pain Relief and of Anesthesia in Disaster Areas"	Harvey C. Slocum, Col., MC
M43–T43	"Water and Electrolyte Balance in Pediatric Anesthesia"	Robert M. Smith, M.D.
M212	"Postanesthesia Recovery Room"	Scott M. Smith, M.D.
M411–T19	"Fluid and Electrolyte Therapy for the Surgical Patient"	Harry Statland, M.D.
M67–T112	"Functional Anatomy of the Larynx"	C. R. Stephen, M.D.
T67	"Anti-Cholinergic Drugs"	C. R. Stephen, M.D.
M211–T65	"Physiology of the Autonomic Nervous System"	Vergil K. Stoelting, M.D.
T411	"Plasma Volume Expanders"	Arthur B. Tarrow, Lt. Col., MC
M68–T68	"Fire and Explosion Hazards in Hospitals and Their Control"	Geroge J. Thomas, M.D.
M65–T21	"Pulmonary Function Tests"	F. H. Van Bergen, M.D.
M10–T41	"The Physiology of Circulation as Related to Anesthesia"	LeRoy Vandam, M.D.
M610–T610	"The Coronary Arterial Blood Flow"	LeRoy Vandam, M.D.
M21–T211	"Hypothermia for Surgery"	Robert Virtue, M.D.
M52–T510	"Positive Pressure Breathing"	Willis G. Watrous, M.D.