REFERENCES

1. Andersen N: Changes in intragastric pressure following the administration of suxamethonium. Brit J Anaesth 34:363, 1962
2. Roe RB: The effect of suxamethonium on intragastric pressure. Anaesthesia 17:179, 1962
3. Wylie WD: The use of muscle relaxant at the induction of anesthesia of patients with a full stomach. Brit J Anaesth 35:168, 1963
4. La Cour D: Rise in intragastric pressure caused by suxamethonium fasciculations. Acta Anaesth Scand 13:225, 1969
5. Lamoreaux LR, Urbach KF: Incidence and prevention of muscle pain following the administration of succinylcholine. ANESTHESIOLOGY 21:394, 1960
6. Usubiaga JE, Wikinski JA, Usubiaga LE, *et al.*: Intravenous lidocaine in the prevention of postoperative muscle pain caused by succinylcholine administration. Anesth Analg 46:225, 1967
7. Marchand P: A study of the forces productive of gastro-oesophageal regurgitation and herniation through the diaphragmatic hiatus. Thorax 12:189, 1957
8. Schoenstadt DA, Whitcher CE: Observation on the mechanism of succinylcholine-induced cardiac arrhythmia. ANESTHESIOLOGY 24: 358, 1963
9. Greenan J: The cardio-oesophageal junction. Brit J Anaesth 33:432, 1961
10. Marchand P: The gastro-oesophageal "sphincter" and mechanism of regurgitation. Brit J Surg 42:504, 1955
11. Walts LF, Dillion JB: Clinical studies of the interaction between *d*-tubocurarine and succinylcholine. ANESTHESIOLOGY 31:39, 1969
12. Katz RL, Katz GJ: Complications associated with the use of muscle relaxants, Muscle Relaxants, Clinical Anesthesia. Edited by FF Foldes. Philadelphia, FA Davis, 1966, pp 125
13. La Cour D: Prevention of rise in intragastric pressure due to suxamethonium fasciculations by prior dose of *d*-tubocurarine. Acta Anaesth Scand 14:5, 1970
14. Miller RD, Way WL, Hickey RF: Inhibition of succinylcholine-induced increased intraocular pressure by nondepolarizing muscle relaxants. ANESTHESIOLOGY 29:123, 1968
15. Wikinski R, Usubiaga LJ, Usubiaga JE, *et al.*: Prevention of succinylcholine fasciculations with local anesthetics. ANESTHESIOLOGY 26: 3, 1965

CASE REPORTS

Malignant Hyperthermia Associated with Hypocalcemia

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Hyperthermia *following* anesthesia has been a matter of concern for decades. Typically the rise in temperature was slow and progressive, and usually it was attributed to elevated room temperature, heavy draping, or prolonged surgery. Recent reports from Australia, Canada, the United States, Great Britain, and South Africa have described a more alarming type of hyperthermia, which occurs during anesthesia.[1-22] This condition, which occurs in both man and animals, appears to be biphasic. The initial phase is characterized by an insidious, progressive rise in temperature, accompanied by appropriately profuse sweating. A prodrome of progressive muscular rigidity may be present but is often unrecognized because of surgical draping.

The early phase, which occurs 30 to 90 minutes after induction, is followed by a more rapid rise in temperature accompanied by inability to sweat and mottling of the skin. Studies made immediately upon recognition of the syndrome reveal severe metabolic and respiratory acidosis and extreme alterations in arterial-to-mixed venous oxygen ratios. Bradycardia progressing to cardiac arrest usually follows; on occasion, this has responded to intravenous calcium chloride. Disseminated intravascular coagulation may be detected fol-

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lowing the rise in temperature. The syndrome has been called malignant hyperthermia.

Malignant hyperthermia, in both man and animals, appears to have a genetic basis.[1-4, 12, 13, 16-19, 33-37] Inheritance is thought to be autosomal dominant, with reduced penetrance and variable expressivity.[34] A recent study[33] estimates the incidence to be 1:10,000, with a range of 1:5,000 to 1:70,000. Patient ages have ranged from 6 months[17] to 58 years.[32] The earliest reported cases may have occurred as early as 1922,[3] but recent case-reporting suggests that the increased incidence of malignant hyperthermia has paralleled the development and use of more potent anesthetics. The mechanism by which the potent anesthetics "trigger" this condition is unknown; several etiologies will be considered. Hyperpyrexia associated with nonanesthetic (*i.e.*, psychotropic) drugs may offer some insight.

In all cases of malignant hyperthermia, electrolyte abnormalities have been found. The following case history will present the rarely seen association of hypocalcemia and hyperkalemia.

Report of a Case

A 23-year-old Caucasian man was admitted to the hospital with a history of chronic anterior dislocation of the right shoulder. The remainder of the history was negative except for a history of drug abuse involving agents described only as "pot," "LSD," and "speed." Preoperative examination and laboratory studies, including determination of calcium and phosphorus, disclosed no abnormalities (table 1).

The patient was given atropine, 0.4 mg, and meperidine (Demerol), 50 mg, intramuscularly and taken to the operating room for a Putti-Platt repair of the right shoulder. Anesthesia was induced with thiopental sodium (Pentothal), 375 mg (fig. 1). Despite intravenous injection of 100 mg succinylcholine, relaxation of the mandible was incomplete and intubation somewhat difficult. Anesthesia was maintained with a mixture of halothane and 50 per cent nitrous oxide–oxygen. Approximately 45 minutes after induction, the heart rate and respiratory rate began a steady increase. Ninety minutes after induction, the patient became markedly tachypneic and was noted to have a cape-like distribution of cyanotic color, with distention of the neck and forehead veins. Breath sounds over the left anterior chest appeared diminished, and the endotracheal tube was removed. Ventilation seemed to improve.

The patient remained tachypneic, however, and the soda-lime canister was changed. Systolic blood pressure was 90 mm Hg. Two attempts at reintubation were made, of which the second was successful. A total of 0.8 mg atropine and 120 mg succinylcholine, in divided dosage, was needed. During auscultation of the chest to assess the effect of intubation, the skin was noted to be hot, and the soda–lime canister was found to be markedly heated. The drapes were quickly removed, to reveal the lower extremities in a severe state of extensor hypertonus and the hands clenched in fists. The anesthetic was discontinued and 100 per cent oxygen given. A rectal thermistor probe revealed a temperature of 106.5 F.

Table 1. Laboratory Data, Electrolytes

	Ca^{++} (mEq/l)	PO_4 (mg/100 ml)	K^+ (mEq/l)
Preoperative	(9.5 mg/100 ml)	4.3	
At peak of temperature rise	3.8	11.3	7.4
After cooling			6.1
	3.8	6.8	5.8
			6.2
	3.5	8.2	6.4
			6.4
	3.7		7.2

Cooling procedures were begun immediately, with iced Ringer's lactate solution given intravenously and gastric lavage with iced saline solution. A polyethylene sheet was placed under the patient and he was "covered" with crushed ice. The temperature continued to rise, and the patient developed profound bradycardia and hypotension. The blood pressure and pulse were unresponsive to ephedrine and mephentermine, but returned after 400 mg $CaCl_2$.

Blood samples taken at the peak of the temperature rise, after removal of the soda–lime canister and administration of five ampules (220 mEq) of sodium bicarbonate, had a P_{CO_2} of 65 mm Hg, a P_{O_2} of 350 mm Hg, and *p*H of 7.2. Serum electrolytes at that time showed marked hyperkalemia (7.4 mEq/l), hyperphosphatemia (11.3 mg/100 ml), and hypocalcemia (3.8 mEq/l) (table 1).

The temperature fell rapidly to 100 F (fig. 1). Within an hour, the temperature was 99 F, and meperidine (Demerol) and chlorpromazine (Thorazine) were given to prevent shivering. During cooling, supraventricular arrhythmias were encountered, but they responded readily to four doses of 0.5 mg each of propranolol, given intravenously.

Blood began to ooze from the surgical incision, the nose, and the sites of intravenous and intramuscular puncture. Clotting studies revealed no clotting at one hour; prothrombin time 27 sec; partial thromboplastin time 93 sec; fibrinogen 77

mg; factor II 30 per cent, factor V 8 per cent, factor VIII 15 per cent, factor X 15 per cent, and factor XI 4 per cent; platelet count 159,000. The patient was given heparin intravenously at four-hour intervals and the bleeding progressively diminished. Hypotension, accompanied by low central venous pressure (0–3 cm H_2O) and low cardiac (3.2 l/min), necessitated the administration of blood and other fluids. The central venous pressure was kept between 8 and 16 cm H_2O.

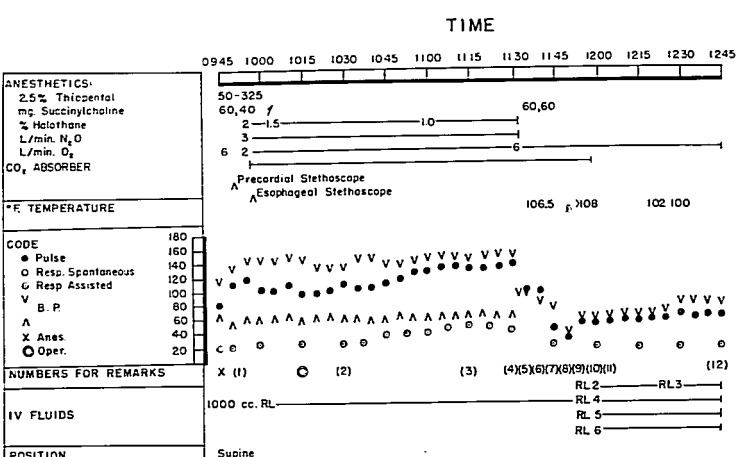
Electrolytes in serially sampled blood (table 1) revealed persistent hyperkalemia, hyperphosphatemia, and hypocalcemia. Treatment consisted of regular insulin intravenously, Kayexalate enemas, and calcium chloride intravenously. The hands, still clenched, responded to 900 mg of $CaCl_2$ at hour 16, but the general state of hypertonus persisted.

About 24 hours after induction, bleeding at the sites of puncture and surgical incision increased, accompanied by gastrointestinal hemorrhage and hemoptysis. Additional heparin, blood and plasma were administered and, because of the suspected presence of fibrinolysis, a single injection of ethyl-aminocaproic acid (Amicar), 5.0 g, was given.

Pulmonary inspiratory pressures progressively increased to a preterminal level of 60 cm H_2O. Prior to death, Pa_{O_2} fell to 40 mm Hg (FI_{O_2} 1.0), and the patient died following a ventricular arrhythmia.

Analysis of the halothane in this case showed the presence of nitrous oxide and a large amount of thymol (44 times normal). Vapor-phase chromatography revealed no single minor impurity present to an extent greater than five parts per million.

Pathology Report. Gross examination revealed diffuse muscular edema and hemorrhage, hemorrhagic tracheitis, pulmonary congestion and hemorrhage, and melena. Microscopic studies revealed only a few widely scattered fibrin thrombi; there was no evidence of muscular destruction.



REMARKS: (1) Relaxation of mandible incomplete, intubation somewhat difficult. *(2)* Skin warm. *(3)* Noted to have a cape-like suffuse cyanotic color with distention of the neck veins. *(4)* Breath sounds over left anterior chest appeared diminished. The endotracheal tube removed. Ventilation appeared to improve. *(5)* Soda lime canister changed. *(6)* Patient remained tachypneic, and two attempts at reintubation were made; the second attempt was successful (0.8 mg. atropine and 120 mg. succinylcholine, divided dosage). *(7)* Patient and soda lime canister noted to be hot, hyperrigidity present, rectal probe revealed temperature 106.5°F. *(8)* Ephedrine 25 mg. I.V., mephentermine 15 mg. I.V. *(9)* 400 mg. calcium chloride. 3000 cc iced ringer's lactate started I.V. Polyethylene sheet placed under patient; covered with ice. *(10)* Five ampules sodium bicarbonate. Put on non rebreathing system. *(11)* blood gases, electrolyte studies drawn. *(12)* meperidine (50 mg.) and chlorpromazine (12.5 mg.) I.V. to prevent shivering. Patient transferred to recovery room.

23 year old male with chronic anterior dislocation of right shoulder. Wt. 167 lbs., hematocrit 46, I.M. pre-op medication 0.4 mg. atropine and 50 mg. meperidine.

Agent and technique: Halothane - N_2O O_2; Endotracheal tube 9mm with 6cc cuff, oral airway.

Operation: Putti-platt repair, right shoulder — Total Fluids: 900 cc RL, 4400 cc iced RL — EBL: 300 cc

FIG. 1. Anesthetic record.

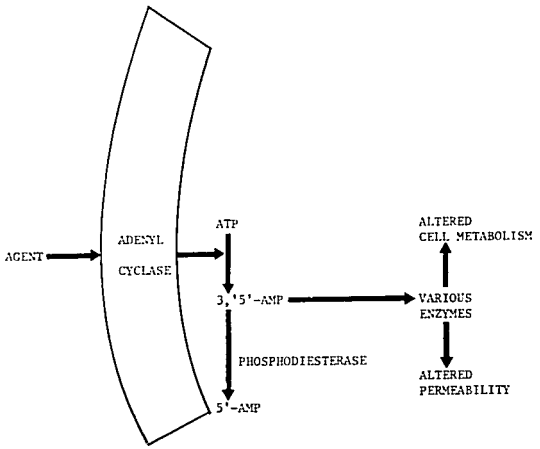


FIG. 2. Cyclic AMP: formation and cellular effects (after Sutherland).

DISCUSSION

The case history illustrates some of the classic signs and metabolic derangements found in malignant hyperthermia. The history of drug abuse and the presence of hypocalcemia deserve particular comment; a prerequisite, however, is a discussion of the possible etiologies of malignant hyperthermia.

Malignant hyperthermia appears to be a metabolic disorder, the specific defect remaining unknown. Wilson and co-workers[38] suggested that the defect lies in the coupling of oxidative phosphorylation. They used as a model an uncoupling agent, 2,4-dinitrophenol (DNP),[39] thought to act at the mitochondrial membrane.[40] Wilson[38] showed, in the dog, that the uncoupling produced by the administration of DNP is enhanced by halothane–oxygen but not by pentobarbital–oxygen. Similarly, Snodgrass incubated a number of hydrocarbons with normal rat liver mitochondria and demonstrated uncoupling of oxidative phosphorylation by chloroform, diethyl ether, and halothane.[41]

Other investigators question the association between uncoupling and malignant hyperthermia.[33, 42-45] They suggest that other pathways are involved instead. One pathway, not previously mentioned, involves adenosine 3,5'-monophosphate (3,5'-AMP, cyclic AMP, cAMP). Cyclic AMP is formed from ATP (fig. 2)[46]; the reaction is catalyzed by adenyl cyclase, an enzyme "fixed" to the cell membrane[47, 48] and found in all animal tissues, including muscle, liver, and brain.[49] Adenyl cyclase is activated by numerous hormones, including the catecholamines and the xanthines; activation by other agents is suspected.[46, 50]

Cyclic AMP, if not inactivated by phosphodiesterase, acts as a "messenger" within the cell, stimulating a number of enzyme systems and altering cellular metabolism and cell permeability.[46]

The effect of some psychotropic drugs on the cyclic AMP system is now established. A recent report by Abdulla and Hamadah clearly demonstrates that dibenzazepine (tricyclic) antidepressants (table 2) inhibit the degradation of cyclic AMP. They suggest that these drugs are potent competitive inhibitors of phosphodiesterase and exert their antidepressive effect by increasing intracellular levels of cyclic AMP.[51] Monoamine oxidase inhibitors (MAOI; table 2) also appear to increase intracellular cyclic AMP, elevating catecholamines, which in turn stimulate adenyl cyclase.

TABLE 2. Some Antidepressant Drugs, Many Associated with Hyperpyrexia

Dibenzazepine compounds
Amitriptyline (Elavil)
Desmethyl imipramine (Norpramin)
Imipramine (Tofranil)
Nortriptyline (Aventyl)
Protriptyline (Vivactil)
Monoamine oxidase inhibitors (MAOI's)
Isocarboxazid (Marplan)
Nialamide (Niamid)
Phenelzine (Nardil)
Tranylcypromine (Parnate)

By increasing intracellular cyclic AMP, these drugs might in some instances be expected to produce a hypermetabolic state. Indeed, several cases of hyperpyrexia and muscular rigidity have followed the combined use of tricyclic antidepressants and MAOI.[52-60] Usually the patient is in his late twenties. About 6–36 hours after the administration of combined therapy, delirium, sweating, and hyperpyrexia develop, followed or accompanied by muscular hyperrigidity, coma and, occasionally, spasm. Mortality is high; about 60–70 per cent do not survive.

The syndrome induced by psychotropic drugs appears similar to that which follows administration of potent anesthetics. A common metabolic pathway may be involved. In psychotropic drug-induced hyperpyrexia, phosphodiesterase activity apparently is depressed in the presence of increased adenyl cyclase activity. In patients susceptible to malignant hyperthermia, phosphodiesterase may be abnormal in amount or structure. The administration of potent general anesthetics may further depress phosphodiesterase activity or may stimulate adenyl cyclase activity, possibly triggering some of the manifestations of malignant hyperthermia.

Serum electrolytes in antidepressant-induced hyperpyrexia have not been determined, but in malignant hyperthermia, hyperkalemia is a frequent finding. Hypocalcemia, less frequently reported but suspected on clinical grounds, is also reported. Purkis[18] describes a 44-year-old woman with carpopedal spasm, ECG changes, bradycardia, and hypotension following the development of malignant hyperthermia; calcium levels were within normal limits, but the patient responded favorably to administration of calcium chloride. Still other case reports describe the presence of bradycardia, frequently amenable to calcium chloride.[10, 18, 19, 24, 25] Hpocalcemia, though minimal, and hyperphosphatemia were first documented by Cody.[22] Abnormal calcium and phosphate levels were present in our patient (table 1) from immediately following recognition of the syndrome to death 27 hours following induction. Recently, Denborough[61] reported marked hypocalcemia and hyperphosphatemia in a 54-year-old man with malignant hyperthermia. The presence of hypocalcemia is not readily explained and, in fact, conflicts with data recorded during studies of the Landrace pig.[45, 62] Jones and Burnap, however, studying an inbred strain of Poland China swine have found lowered levels of plasma calcium and magnesium on the *in vitro* exposure of this susceptible breed's muscle to halothane.[67] Recent studies have elucidated the role of cyclic AMP in the metabolism of calcium and, in turn, the role of calcium in muscle contractility[63, 66]; clarification of the changes in malignant hyperthermia will require further study.

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REFERENCES

1. Burford GE: Hyperthermia following anesthesia: A consideration of control of body temperature during anethesia. ANESTHESIOLOGY 1:208, 1940
2. Locher WG: Fulminant hyperpyrexia associated with anaesthesia. Anaesthesia 23:253, 1968
3. Denborough MA, Lovell RRH: Anaesthetic deaths in a family. Lancet 2:45, 1960
4. Denborough MA, Forster JFA, Lovell RRH, *et al.*: Anaesthetic deaths in a family. Brit J Anaesth 34: 395, 1962
5. Ruttle LD: Death occurred in the operating room following extreme hyperthermia during an elective cholecystectomy. Amer Soc Anesth Newsletter, July 1962, p 21
6. Saidman LJ, Havard ES, Eger EI II: Hyperthermia during anesthesia. JAMA 190:1029, 1964
7. Niesen WC: Hyperthermic episodes following surgery. JAMA 191:1082, 1965
8. Relton JES, Creighton RE, Johnston AE, *et al.*: Hyperpyrexia in association with general anaesthesia in children. Canad. Anaesth Soc J 13:419, 1966

9. Thut WH, Davenport HT: Hyperpyrexia associated with succinylcholine-induced muscle rigidity: A case report. Canad Anaesth Soc J 13:425, 1966
10. Hogg S, Renwick W: Hyperpyrexia during anesthesia. Canad. Anaesth Soc J 13:429, 1966
11. Cullen WG: Malignant hyperpyrexia during general anaesthesia: A report of two cases. Canad Anaesth Soc J 13:439, 1966
12. Lavoie G: Hyperpyrexia during general anaesthesia: A case report. Canad Anaesth Soc J 13:444, 1966
13. Davies LE, Graves HB: Hyperpyrexia and death associated with general anesthesia. Canad Anaesth Soc J 13:447, 1966
14. Carpenter CG, Auerbach VH, DiGeorge AM, *et al.*: Rhabdomyolysis after routine administration of succinylcholine in children. Soc Pediat Res, 36th Annual Meeting, Atlantic City, N. J., April 29–30, 1966, p 175
15. Stephen CR: Fulminant hypthermia during anesthesia and surgery. JAMA 202:178, 1967
16. Wilson RD, Dent TE, Traber DL, *et al.*: Malignant hyperpyrexia with anesthesia. JAMA 202:183, 1967
17. Cleveland Anesthesia Study Commission: Case report number 303. Amer Soc Anesth Newsletter, March 1967, p 6
18. Purkis IE, Horrelt O, deYoung CG, *et al.*: Hyperpyrexia during anesthesia in a second member of a family, with associated coagulation defect due to increased intravascular coagulation. Canad Anaesth Soc J 14:183, 1967
19. Relton JE, Creighton RE, Conn AW: Fulminane hyperpyrexia associated with anaesthesia. Anaesthesia 23:253, 1968
20. Ruscio JR, Morcus PS: Sudden hyperthermia during anesthesia. Surg Clin N Amer 48: 415, 1968
21. Jensen K, Bennike K-AA, Hansel HK, *et al.*: Myoglobinuria following anaesthesia including suxamethonium. Brit J Anaesth 40:329, 1968
22. Cody JR: Muscle rigidity following administration of succinylcholine. ANESTHESIOLOGY 29:159, 1968
23. Fulminating Hyperthermia during Anesthesia. Clinical Anesthesia Conference, New York State Society of Anesthesiologists, New York, New York. New York J Med 68:2566, 1968
24. Britt BA, Gordon RA: Three cases of malignant hyperthermia with special consideration of management. Canad Anaesth Soc J 16: 99, 1969
25. Gibson JA, Gardiner DM: Malignant hypertonic hyperpyrexia syndrome. Canad Anaesth Soc J 16:106, 1969
26. Thomford NR, Hamelberg WE, Wiederholt WC: Sudden hyperpyrexia during general anesthesia. Surgery 66:850, 1969
27. Daniels JC, Polayes IM, Villar R, *et al.*: Malignant hyperthermia with disseminated intravascular coagulation during general anesthesia: A case report. Anesth Analg 48:877, 1969
28. Capizzi LS, Phillips OC, Harry LC: Malignant hyperthermia during anesthesia. ANESTHESIOLOGY 31:97, 1969
29. Murray BRP, Williams PAD: Malignant hyperpyrexia during anesthesia for colectomy. Brit Med J 1:488, 1969
30. Davies RM, Packer KJ, Titel J, *et al.*: Malignant hyperpyrexia. Brit J Anaesth 41:703, 1969
31. Satnick JH: Hyperthermia under anesthesia with regional muscle flaccidity. ANESTHESIOLOGY 30:472, 1969
32. Ryan JF, Papper EM: Malignant fever during and following anesthesia. ANESTHESIOLOGY 32:196, 1970
33. Britt BA, Kalow W: Hyperrigidity and hyperthermia associated with anesthesia. Ann NY Acad Sci 151:947, 1968
34. Britt BA, Locher WG, Kalow W: Hereditary aspects of malignant hyperthermia. Canad Anaesth Soc J 16:89, 1969
35. Hall LW, Woolf N, Bradley JWP, *et al.*: Unusual reaction to suxamethonium chloride. Brit Med J 2:1305, 1966
36. Harrison GG, Biebuyck JF, Terblanche J: Hyperpyrexia during anaesthesia. Brit Med J 3:594, 1968
37. Harrison GG, Saunders SJ, Biebuyck JF, *et al.*: Anaesthetic-induced malignant hyperpyrexia and a method for its prediction. Brit J Anaesth 41:844, 1969
38. Wilson RD, Nichols RJ Jr, Dent TE, *et al.*: Disturbances of the oxidative-phosphorylation mechanism as a possible etiological factor in sudden unexplained hyperthermia occurring during anesthesia. ANESTHESIOLOGY 27:231, 1966
39. Vorbrodt A: The effect of some inhibitors of oxidative phosphorylation on the histochemically demonstrable phosphatases. Exp Cell Res 12:154, 1957
40. Brierley GP, Stoner CD: Swelling and contraction of heart mitochondria suspended in ammonium chloride. Biochemistry 9:708, 170
41. Snodgrass PJ, Piras MM: The effects of halothane on rat liver mitochondria. Biochemistry 5:1140, 1966
42. Viguera MG, Conn AW: An investigation of general anaesthesia and hyperpyrexia in chickens. Canad Anaesth Soc J 14:193, 1967
43. Challoner DR: Hypermetabolic states. Lancet 2:681, 1966
44. Wang JK, Moffit EA, Rosevear JW: Oxidative phosphorylation in acute hyperthermia. ANESTHESIOLOGY 30:439, 1969
45. Berman MC, Harrison GG, Dutoit P, *et al.*:

Halothane-induced hyperpyrexia in Landrace pigs. S Afr Med J 43:545, 1969
46. Sutherland EW, Robison A, Butcher RW: Some aspects of the biological role of adenosine 3,5'-monophosphate (cyclic AMP). Circulation 37: 279, 1968
47. Davoren PR, Sutherland EW: Cellular location of adenyl cyclase in the pigeon erythrocyte. J Biol Chem 238:3016, 1963
48. Oye I, Sutherland EW: Effect of epinephrine and other agents on adenyl cyclase in the cell membrane of avian erythrocytes. Biochem Biophys Acta 127:347, 1966
49. Sutherland EW, Rall RW, Menon T: Adenyl cyclase: I. Distribution, preparation and properties. J Biol Chem 237:1220, 1962
50. Butcher RW: The biological role of adenosine 3,5'-monophosphate (cyclic AMP). Proc Int Union Physiol Sci 51:161, 1968
51. Abdulla YH, Hamadah K: 3,5' cyclic adenosine monophosphate in depression and mania. Lancet 1:378, 1970
52. Luby ED, Domino EF: Toxicity from large doses of imipramine and an MAO inhibitor in suicide intent. JAMA 177: 68, 1961
53. Stanley B, Pal NR: Fatal hyperpyrexia with phenelzine and imipramine. Brit Med J 2: 1011, 1964
54. Brachfeld J, Wirtshafter A, Wolfe S: Imipramine-tranylcypromine incompatibility. JAMA 186:1172, 1963
55. Sargant W: Combining the antidepressant drugs. Brit Med J 1:251, 1965
56. Hills NF: Combining the antidepressant drugs. Brit Med J 1:859, 1965
57. Lee FI: Imipramine overdosage—report of a fatal case. Brit Med J 1:338, 1961
58. Harrer G: Incompatibility between MAO inhibitors and imipramine. Wien Med Wschr 111:551, 1961
59. Babiak W: Case fatality due to overdosage of a combination of tranylcypromine (Parnate) and imipramine (Tofranil). Canad Med Ass J 85:377, 1961
60. Jori A, Garattini S: Interaction between imipramine-like agents and catecholamine-induced hyperthermia. J Pharm Pharmacol 17:480, 1965
61. Denborough MA, Forster JFA, Hudson MC, *et al.*: Biochemical changes in malignant hyperpyrexia. Lancet 1:1137, 1970
62. Pollock RA, Standefer JC, Hildebrandt PK, *et al.*: Unpublished data
63. Chase LR, Melson GL, Aurbach GD: Pseudohypoparathyroidism: Defective excretion of 3,5'-AMP in response to parathyroid hormone. J Clin Invest 48:1832, 1969
64. Holland WC, Porter MT: Pharmacological effects of drugs on excitation—contraction coupling in cardiac muscle. Fed Proc 28: 1663, 1969
65. Bianchi CP: Pharmacology of excitation—contraction coupling in muscle. Fed Proc 28: 1624, 1969
66. Haugaard N, Haugaard ES, Lee NH, *et al.*: Possible role of mitochondria in regulation of cardiac contractility. Fed Proc 28:1657, 1969
67. Jones EW, Burnap TK, Nelson TE, *et al.*: Preliminary studies on fulminant hyperpyrexia in a family of swine. Abstracts of Scientific Papers, ASA meeting, New York, 1970, p 47

Vasospasm with an Indwelling Radial Artery Cannula

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Prolonged cannulation of the radial artery is used in the management of critically ill patients and patients undergoing extensive surgery.[1-5] The purposes and advantages include: 1) it is less traumatic to the vessel than repeated punctures when serial blood samples are necessary; 2) accurate measurement of arterial pressure is obtainable, especially when the use of a pneumatic cuff is unsatisfactory, *e.g.*, with hypothermia, extracorporeal circulation; 3) it may be less disturbing to the patient where apprehension may alter values to be studied, *e.g.*, arterial blood gases, cardiac output. The value of prolonged cannulation may be enhanced by minimizing its complications. This communication reports the response to intra-arterial lidocaine with interruption of blood flow of a hand which showed signs of inadequate circulation distal to the indwelling radial cannula.

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