Anesthesiology
V 36, No 1, Jan 1972

Malignant Hyperthermia of Swine

E. W. Jones, Ph.D., T. E. Nelson, Ph.D.,† I. L. Anderson, M.S.,‡*
D. D. Kerr, B.V.Sc.,§ T. K. Burnap, M.D.¶

Inherited susceptibility to malignant hyperthermia has been recognized in Poland China swine. Clinical and laboratory studies were made to compare the syndrome with that observed in man and in other breeds of swine in South Africa and Europe. Malignant-hyperthermia-susceptible (MHS) swine were identified by increased ATP depletion in biopsied muscle studied *in vitro*. MHS and related swine had elevated serum creatine phosphokinase values compared with control swine (MHS swine $\bar{x}$ 2,435 IU/l; MHS-related swine $\bar{x}$ 1,260 IU/l; control swine $\bar{x}$ 144 IU/l). The syndrome was triggered by administration of halothane and of succinylcholine chloride. Resulting clinical responses, in order of appearance, were tachycardia, hyperventilation, skeletal muscle rigidity, hyperthermia, cardiac arrhythmias, and death. Blood chemical responses which occurred early in the syndrome included hypercapnia, acidosis, elevated plasma inorganic phosphorus, and lactacidemia. The malignant hyperthermia syndrome in this breed of swine appears similar to that in Landrace and Pietrain swine, and in man. The Poland China swine is an appropriate animal model for the study of this disease. (Key words: Malignant hyperthermia; Swine; Halothane; Succinylcholine chloride.)

* Professor of Medicine and Surgery, College of Veterinary Medicine, Oklahoma State University.
† Research Associate, College of Veterinary Medicine, Oklahoma State University.
‡ Assistant Professor of Medicine and Surgery, College of Veterinary Medicine, Oklahoma State University. Present address: Veterinary Medicine, Massey University, Palmerston North, New Zealand.
§ Graduate Research Assistant, College of Veterinary Medicine, Oklahoma State University.
¶ Professor of Anesthesiology, University of Texas S. W. Medical School, Dallas, Texas. Present address: Department of Anesthesiology, Parkway Hospital, Boston, Massachusetts.
Received from the College of Veterinary Medicine, Oklahoma State University, Stillwater, Oklahoma 74074. Accepted for publication July 18, 1971. Supported in part by the Oklahoma Agricultural Experiment Station, USPHS General Medical Research Grant FR-05567, and Ayerst Laboratories, New York, New York. Presented at the annual meeting of the American Society of Anesthesiologists, New York, New York, October 21, 1970.

SINCE MALIGNANT HYPERTHERMIA is frequently fatal in man,[1] it is fortunate that naturally occurring models for the study of this syndrome have been recognized in certain families of swine.[2] Malignant hyperthermia has been found in Landrace swine in England[3] and South Africa[4]; in Pietrain swine in the Netherlands[5] and England[6]; and possibly in Large White swine in England.[6]

The syndrome has been triggered in swine by succinylcholine chloride,[3, 4] chloroform,[4] halothane,[3, 6] and physiologic stress.[5, 6] In some swine more than one challenge has been necessary to induce a positive response.[6] Thiopental sodium and nitrous oxide have not been effective as triggering agents.[4]

Breeding records of Landrace swine suggest that, as in man, the predisposition to malignant hyperthermia is inherited as an autosomal dominant, although a few sporadic instances have been encountered in unrelated animals.[7] Susceptible swine have been selected not only by their pedigrees, but also by elevated serum creatine phosphokinase (CPK) values,[7, 8] elevated serum aldolase activity,[8] and increased depletion of muscle adenosine triphosphate (ATP) *in vitro*.[4]

Administration of a "triggering" agent to susceptible swine results in tachypnea, hyperventilation, muscular rigidity, blotchy cyanosis of the skin, tachycardia, and a rapid progressive rise in the core temperature to 42 to 45 C or more.[3-6] Terminally, ventricular arrhythmias, gross bradycardia, and asystole 10 to 165 ($\bar{x}$ 106) minutes after exposure to the triggering agent have been reported.[4]

Study of one Landrace pig during malignant hyperthermia[9] revealed elevations of plasma protein, sodium, calcium, magnesium, potassium, and inorganic phosphorus, and blood glucose, lactate, and Pa_{CO_2}. Oxygen consumption and carbon dioxide output were also increased, and the respiratory quotient was high

(1.69). Lactacidemia[5, 6] and increased inorganic phosphorus values[6] in malignant hyperthermia of Pietrain swine have been reported.

Minimal postmortem changes have been reported.[4, 6] Considerable variation in the depth of color of different skeletal muscles has been described,[6] and many of the skeletal muscles have contained moderate numbers of rounded hyaline fibers with apparent loss of striation.[6]

Harrison *et al.*[4] considered the syndrome which they observed in Landrace swine to be the same explosive thermal idiosyncrasy to anesthesia as that which occurs in man. The present report describes malignant hyperthermia observed in Poland China swine in this country, thereby permitting comparison with that reported in other breeds of swine and in man.

Methods

Malignant hyperthermia was discovered in purebred Poland China swine during halothane anesthesia of sows for procurement of germfree swine. Susceptible swine were thereafter procured by purchasing related animals. Subsequently, susceptible swine have been identified from breeding records, by measuring the depletion of muscle ATP during exposure to halothane *in vitro* according to the method of Harrison *et al.*,[4] and by determination of plasma CPK values. Control, unrelated swine were obtained from the Oklahoma State University swine herd and similarly treated.

Eight- to 16-week-old swine were maintained and anesthetized in a controlled environment (*circa* 72 F) and fed a commercially available diet[**] *ad lib*. All swine were immunized with killed *Leptospira pomona*[††] and *Erysipelothrix insidiosa*[‡‡] vaccines, and were treated at monthly intervals for the control of external (rotenone) and internal parasitism (dichlorvos).[§§] Food was withheld for approximately 12 hours prior to induction of anesthesia.

During initial efforts to detect susceptible swine, anesthesia was induced and maintained with halothane and oxygen via a nonrebreathing system. Subsequently, anesthesia was induced by thiamylal sodium, iv, the tracheas of the swine were intubated, and nitrous oxide and oxygen were administered via a nonrebreathing system. This procedure permitted biopsy of the longissimus dorsi muscle and monitoring prior to administration of halothane or other triggering agents. Physiologic saline solution (200–300 ml) was administered intravenously during the course of anesthesia.

Central venous and arterial pressures were monitored via 5½-inch, 16-gauge teflon cannulas in the anterior (superior) vena cava and the femoral artery, using Statham pressure transducers. Esophageal and rectal temperatures were measured by thermistor probes, and lead II of an electrocardiograph was used to monitor cardiac rate and rhythm. Respiratory rate and minute volume were determined by a respiration monitor.[¶¶]

Routine hemograms were obtained prior to induction of anesthesia. Blood gas and *p*H determinations were made at 38 C with P_{O_2} and P_{CO_2} microelectrodes and a Radiometer model 27 *p*H meter. Serum creatine phosphokinase (CPK),[10] plasma glucose, and blood pyruvate and lactate[11] levels were determined enzymatically. Plasma inorganic phosphorus was determined by the method of Fiske and Subbarrow,[12] and calcium, magnesium, and potassium were measured by atomic absorption spectrophotometry. Venous blood samples were used to measure coagulation,[13] partial thromboplastin[14] and prothrombin times,[15] clot retraction,[16] and platelet count.[17]

After pre-challenge data had been obtained, the swine received 1 per cent halothane and oxygen for 30 minutes. Post-challenge data were recorded either continuously or at 5-minute intervals. When no positive response had occurred after 30 minutes, the halothane concentration was increased to 2 per cent or more. In the event of severe hypotension and apnea, the pig was resuscitated by manual compression of the rebreathing bag and halothane administration was discontinued. When spon-

[**] Acco Pork Maker Pellets, Acco Feeds, Abilene, Texas.

[††] LeptoVac-P, Norden Company, Box 658, Ft. Worth, Texas.

[‡‡] Erysipelothrix Bacterin, Diamond Laboratories, Wichita, Kansas.

[§§] Atgard-V, Shell Chemical Company, New York, New York.

[¶¶] Chemetron Corp., National Cylinder Gas Division, Chicago, Illinois.

TABLE 1. Clinical and Blood Chemical Responses in Swine Susceptible to Malignant Hyperthermia after Inhalation of Halothane and Oxygen

Response	Minutes until Onset after Halothane Administration	Value Prior to Triggering	Maximal Response after Triggering
Heart rate	28.5 ± 21.1 (1–63)*	111 ± 31 (68–162)	> 258 ± 42 (196–>300)
P_{aCO_2}	31.4 ± 24.4 (5–75)	40 ± 5 (32–47)	>145 ± 52 (58–>190)
Arterial pH	31.4 ± 24.4 (5–75)	7.37 ± 0.08 (7.22–7.48)	<6.88 ± 0.16 (7.25–<6.8)
Plasma P_i	33.0 ± 23.6 (10–70)	9 ± 0.9 (7.4–10)	14.3 ± 2.9 (9.6–17.8)
Blood lactate	37.0 ± 25.0 (10–70)	19.1 ± 11 (8.9–37.1)	61.5 ± 19.4 (37.6–93.1)
Hyperventilation	39.6 ± 31.4 (15–88)	25 ± 15 (12–60)	34 ± 20 (12–75)
		5.25 ± 3.5 (2–13)	11.8 ± 2.7 (8–15)
Muscle rigidity	39.6 ± 26.0 (5–87)		
Hyperthermia	42.0 ± 24.8 (12–90)	38.5 ± 0.6 (38.0–39.9)	43.2 ± 2.16 (39.0–>45.0)
Arrhythmias	47.0 ± 25.8 (15–82)	—	—
Apnea	48.7 ± 25.0 (10–85)	—	—
Death	99.6 ± 31.5 (50–155)*	—	—

* Mean ± SD. Ranges are given in parentheses.

taneous respiration recurred, administration of halothane and oxygen was continued. The experiment was terminated after halothane had been administered for an hour. Control swine were similarly treated.

In susceptible animals, halothane administration was terminated when any two responses indicative of malignant hyperthermia (table 1) occurred. No treatment of the halothane-induced malignant hyperthermia was attempted, and respiration was assisted only during periods of apnea.

Results

Susceptible Poland China swine all had greater than normal depletion of ATP of biopsied muscle during exposure to halothane and carbogen *in vitro*.[18] Serum CPK values were elevated in all susceptible Poland China swine and in related swine (table 2). Clinical signs of malignant hyperthermia usually occurred in the following sequence: tachycardia, hyperventilation and tachypnea, muscular rigidity, hyperthemia, cardiac arrhythmias, apnea, death (table 1).

TABLE 2. Serum Creatine Phosphokinase in Control, MHS* and MHS-related Swine

	CPK (IU/l)
Controls (n = 20)	144 ± 64 (90–492)†
MHS swine (n = 7)	2,435 ± 1,743 (627–5,220)
MHS-related swine (n = 27)	1,260 ± 522 (530–2,989)

* Susceptible to malignant hyperthermia.
† Mean ± SD. Ranges are given in parentheses.

CARDIOVASCULAR SYSTEM

Tachycardia was the initial clinical sign of malignant hyperthermia in seven susceptible swine to which halothane was administered. After initial tachycardia, the heart rate decreased to pretreatment values, only to increase again terminally in four of these seven pigs. In three other fatal cases, heart rate increased progressively up to the terminal stages of the syndrome. In one animal which survived, halothane was administered two times 30 minutes apart; transient tachycardia concomitant with muscular rigidity occurred after each challenge. Tachycardia was not observed during halothane anesthesia of nonsusceptible swine.

Electrocardiography during malignant hyperthermia revealed progressive depression of the S-T segment, increased T-wave amplitude, ventricular extrasystoles, bigeminal pulses, and ventricular fibrillation. In some cases the arrhythmias observed initially were transient. Arrhythmias were not observed in control swine receiving 1 to 2 per cent halothane with oxygen.

Arterial blood pressure usually declined during halothane challenge and subsequent hyperthermia. Transient hypertension (mean arterial blood pressure 200 mm Hg) occurred in two animals. Mean arterial blood pressure declined after administration of halothane to control animals.

RESPIRATORY SYSTEM

The occurrence and time of onset of tachypnea and hyperventilation were variable (table 1). In some swine transient apnea, necessitat-

ing brief mechanical respiration, occurred prior to hyperventilation.

Administration of halothane to control swine depressed respiration. Hypopnea and apnea occurred when 2 per cent or more halothane with oxygen was inhaled.

Skeletal Muscle

The characteristics and onset of muscular rigidity were variable. Rigidity (table 1) was a relatively early sign. It was observed at the same time as initial tachycardia in three pigs, and immediately after the onset of tachycardia in three others. In the remaining two animals rigidity did not develop until 30 to 40 minutes after the appearance of malignant hyperthermia. There were initially coarse localized muscle fasciculations, twitching of one or more digits, and a progressive increase in extensor tone. The rear limbs were usually the first to be affected; later, the rigidity became generalized. Terminally, some swine became partially relaxed.

In control swine muscle relaxation increased progressively with depth of anesthesia.

Temperature

Temperatures often did not decrease after administration of halothane. Temperatures did not increase until after tachycardia and blood chemical changes had occurred (table 1). Once a change had occurred, temperature increases progressed rapidly at 2.4 to 7.9 ($\bar{x}$ 4.0) C/hour (fig. 1).

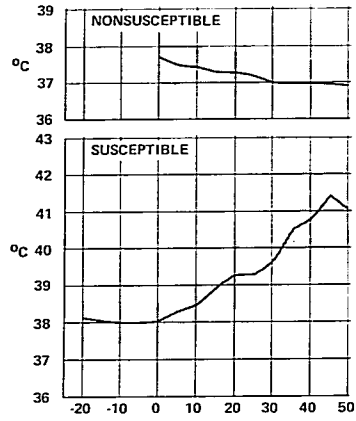


Fig. 1. Rectal temperatures (mean ± SD) after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes.

The temperatures of control swine gradually decreased during halothane administration (fig. 1).

Skin

When pigmentation of the skin permitted, blotchy cyanosis was observed. Skin temperature was variable to the touch, some parts be-

Table 3. Malignant Hyperthermia—Morbidity and Mortality in Susceptible Poland China Swine

Triggering Agent	Number of Susceptible* Swine	Number of Swine Having Malignant Hyperthermia	Number of Deaths Due to Malignant Hyperthermia
Halothane/oxygen			
First exposure	3	3	3
Second exposure	1	1	1
Thiamylal sodium, N_2O/O_2, and halothane			
First exposure	7	7	6
After previous halothane/oxygen	3†	3	3
Thiamylal sodium, N_2O/O_2, and succinylcholine	1	1	1

* Susceptibility determined by the method of Harrison *et al.*[4]
† Two previously challenged once, and one twice, with halothane and oxygen.

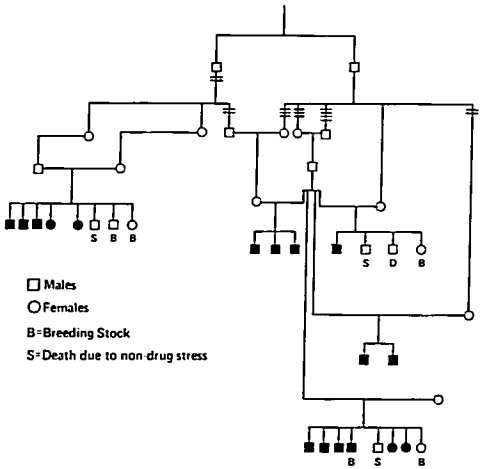


FIG. 2. Familial relationship of malignant-hyperthermia-susceptible Poland China swine. Horizontal lines indicate generations. The eight swine on the left and the eight on the lower right comprise complete litters. Closed circles and squares indicate fatal cases of malignant hyperthermia.

ing hot, others cool; skin over muscular areas was generally warmer than normal.

MORBIDITY AND MORTALITY

Malignant hyperthermia occurred in all 11 male and four female susceptible swine (ages 8 weeks to 10 months) which received halothane or succinylcholine (table 3). Susceptibility was established by determination of the depletion of muscle ATP *in vitro*. Fourteen of 15 swine which developed malignant hyperthermia died. In addition, four susceptible swine died suddenly from exercise and/or stress. One of these, observed just prior to death, had typical clinical signs of malignant hyperthermia. All susceptible swine were obtained from a single family (fig. 2).

POSTMORTEM FINDINGS

No gross lesions were observed, although skeletal muscle was paler than normal. Histologically, there was muscle degeneration in samples taken after the onset of malignant hyperthermia.

LABORATORY FINDINGS

An obvious increase in Pa_{CO_2} (table 1) occurred soon after the initial onset of the syndrome. Maximal Pa_{CO_2}'s occurred terminally in four swine (fig. 3), while in others the degrees of hypercapnia declined prior to death (fig. 3). Arterial *p*H values followed similar trends (fig. 4). Pa_{O_2} values were generally stable, but declined terminally. In control swine, in which respiration was not assisted, there was moderate hypercapnia ($\bar{x}$ 55 ± 13 mm Hg) during deep halothane anesthesia, and arterial pH decreased to 7.23 ± .08 after 60 minutes of halothane anesthesia.

Blood lactate values increased at or just prior to the onset of clinical malignant hyperthermia (table 1, fig. 5). In the one animal in which onset of lactacidemia was delayed, transient malignant hyperthermia was followed by apparent recovery; a second halothane challenge was therefore administered 22 minutes after time zero. In one hog which recovered, lactate increased slightly, from 5.0 to 11.8 mg/100 ml, but returned to normal within 50 minutes. Blood lactate values in control swine remained stable or decreased slightly (fig. 5). Blood pyruvate values were variable, remaining stable or increasing by as much as 100 per cent (fig. 6) within 10–15 minutes after the onset of the clinical syndrome. During halothane anesthesia of con-

trol swine, blood pyruvate values remained unchanged or declined slightly (fig. 6).

Plasma magnesium was 1.4 ± 0.12 mg/100 ml prior to challenge and remained unchanged except in three animals in which increases (10 to 50 per cent higher than values at time zero) occurred after the onset of the clinical syndrome. Plasma magnesium in control swine (1.7 ± 0.10 mg/100 ml) was unchanged during halothane anesthesia. No significant change in plasma calcium concentrations was observed. Values at the time of challenge were 7.7 ± 0.67 (5.4 to 9.4) mg/100 ml. Calcium values in control swine (8.3 ± 0.33 mg/100 ml) remained unchanged throughout halothane maintenance. Plasma inorganic phosphorus values increased just before or just after the onset of clinical disease in three of five fatal cases (fig. 7) in which these values were determined. In the remaining two animals, increases occurred 20–30 minutes after onset of the syndrome. In the hog in which the increase of inorganic phosphorus was delayed, transient malignant hyperthermia was followed by apparent recovery; a second halothane challenge was therefore given. Inorganic phosphorus concentrations in control swine remained stable (fig. 7).

Pre-challenge plasma potassium values were 6.2 ± 1.25 mEq/l and, in five of six swine studied, increased just prior to or during the

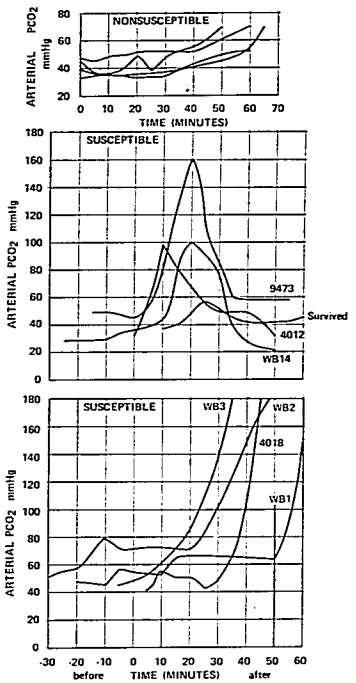


FIG. 3. P_{aco_2} values after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes. Swine WB1, WB2, and WB3 were litter mates, as were 4012, WB14, and the only pig which survived.

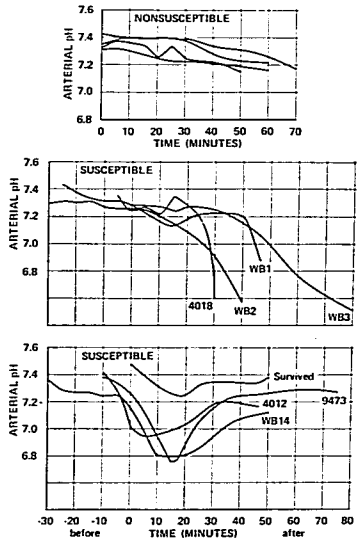


FIG. 4. Arterial *p*H values after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes. Swine WB1, WB2, and WB3 were litter mates, as were 4012, WB14, and the only pig which survived.

onset of malignant hyperthermia. In the remaining hog, this value was unchanged. Elevated serum CPK values in susceptible swine (table 2) increased both during inhalation of halothane and during subsequent malignant hyperthermia (fig. 8). Serum CPK activity in four nonsusceptible swine prior to anesthesia was 226 ± 89 IU/l, and remained unchanged during administration of halothane for an hour. Plasma glucose values increased terminally in four of five fatal cases, and were unchanged in one hog which survived.

Blood coagulation studies (glass clotting time, clot retraction, prothrombin and partial thromboplastin times, and platelet counts) were within normal limits in one susceptible animal studied, and remained unchanged during subsequent malignant hyperthermia.

Discussion

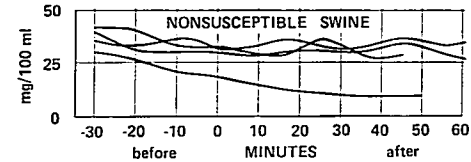
The inheritance and recognition of susceptibility to malignant hyperthermia in Poland China swine would seem to be similar to reported characteristics of Landrace swine in England and in South Africa. While the nature of the inheritance of malignant hyperthermia in Poland China swine has yet to be elucidated, the incidence within the family studied was compatible with an autosomal dominant pattern, but was greater than the 25 per cent incidence reported for Landrace swine.[4]

All susceptible swine studied had increased depletion of muscle ATP when biopsied muscle was exposed to halothane vapor *in vitro*. This technique for recognition of susceptible swine has also been found to be satisfactory in Landrace swine by Harrison *et al.*[4] As in Landrace swine[7] and in human families "at risk,"[19, 20] susceptible and related swine had significantly elevated serum CPK values, which were increased further by the administration of halothane.

Clinical and laboratory findings in malignant hyperthermia of Poland China swine are similar to, if not identical to, those of the human syndrome. Malignant hyperthermia occurred after inhalation of halothane and after injection of succinylcholine chloride. As in man[1] and in Pietrain swine,[6] more than one exposure to halothane was necessary to induce the syndrome in some instances. This may be due to too short a period of administration, insufficient anesthetic concentration, or enhancement of susceptibility by prior exposure. In contrast to the human syndrome and that in Landrace swine, typical malignant hyperthermia was triggered in some swine by restraint and fighting. Similar instances have been reported in Pietrain swine[5, 6]; increased susceptibility to exercise-induced metabolic acidosis has been observed in this breed of swine.[21]

In man, recognition of malignant hyperthermia usually depends upon the occurrence of progressive hyperthermia and muscular rigidity. With the possible exception of succinylcholine-induced malignant hyperthermia, hyperthermia and rigidity in swine were preceded by tachycardia, and often by tachypnea and hyperventilation. It is probable that these early signs (tachycardia, tachypnea, and hyperventilation) are not sufficiently specific to be considered indicative of malignant hyperthermia, although tachycardia and increased ventilation have been said to be early signs in man.[22] While tachycardia occurred initially in all MHS swine in this study, it was found in only 68 of 94 cases in man.[1] In Pietrain swine, Allen *et al.*[6] observed initial cardiac arrhythmias and tachycardia in three fatal cases. The arrythmias observed in this study were similar to those reported for the human syndrome, and although commonly associated with terminal disease, did occur briefly in the initial syndrome in some swine. Initial arrhythmias have also been reported in the human syndrome.[23]

Various degrees of muscular rigidity occurred in all porcine cases observed. Rigidity was first detected either as localized coarse fasciculations or progressive extensor tone, usually of the rear limbs. In some instances, rigidity decreased in the terminal stages, while in others it merged into rigor mortis. Britt and Kalow[1] reported that rigidity was absent or not observed in 23 of 94 human cases. However, detection of muscle rigidity did require careful observation in some swine; rigidity was most readily detected with the animal supine and the limbs unrestrained. In such a position the onset of rigidity with progressive extension of the limbs was readily observed.



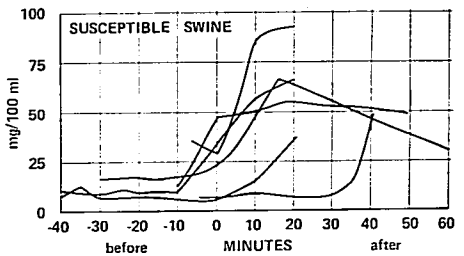


FIG. 5. Blood lactate values after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes.

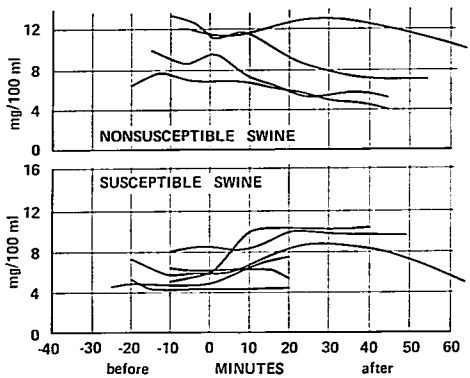


FIG. 6. Blood pyruvate values after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes.

The progressive hyperthermia was similar in swine and human cases reviewed by Britt and Kalow.[1] In view of the lack of treatment of the swine, the temperature increase in man (1.0 to 4.4 $\bar{x}$ 3.4 C/hour)[1] was very similar to that of the swine (2.4 to 7.9 $\bar{x}$ 4.0 C/hour). The variation in skin temperature probably reflected impaired local circulation, indicated by splotchy cyanosis of the skin, an observation likewise recorded for man.[1] Failure to treat the swine may have been responsible for their higher mortality (93 per cent) in contrast to that reported for man (64 per cent).[1] As in man, postmortem findings were relatively insignificant.

Laboratory findings also were comparable to those reported for man[1] and for other swine.[5,6] As in Landrace swine,[9] some blood chemical values (*p*H, P_{CO_2}, lactate, and inorganic phosphorus) changed just at or prior to the appearance of clinical signs and prior to hyperthermia. Some swine were apparently able

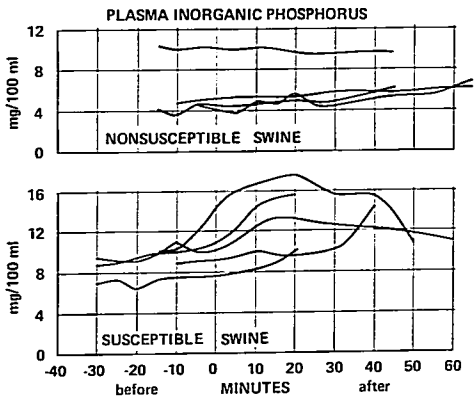


FIG. 7. Plasma inorganic phosphorus values after halothane administration. Onset of malignant hyperthermia in susceptible swine and of halothane administration in nonsusceptible swine is indicated by 0 minutes.

to compensate, presumably by hyperventilation, to a degree sufficient to correct early acidosis and hypercapnia, but died in spite of this (figs. 3 and 4).

Significant changes in serum cation values during porcine malignant hyperthermia have yet to be confirmed. In contrast to the observations of Berman *et al.*,[5] increased plasma calcium and magnesium values were not consistently found. Significant changes in serum calcium values were not found and, as in Pietrain swine,[6] serum magnesium values were increased in some animals only. Plasma calcium and magnesium values, however, were low prior to induction of malignant hyperthermia in the Poland China swine. The significance of these low values and their influence upon subsequent responses have not been determined. Low serum calcium values ($\bar{x}$ 7.8, range 3.5–15.0 mg/100 ml) have been reported in nine of ten human cases.[1] Serum potassium values likewise seem to vary. Hyperkalemia occurred in most cases studied in this series, while Allen *et al.*[6] found hyperkalemia in only two of seven Pietrain swine with malignant hyperthermia. In man, hyperkalemia was found in 16 cases, while potassium values were normal or low in seven others; these values may have been affected by treatment.[1]

Although plasma glucose concentrations varied, and increased terminally, values were generally compatible with those reported in Landrace and Pietrain swine.[6, 9]

Blood coagulation studies in one pig were normal, in contrast to reports of consumption coagulopathies in some human cases.[1]

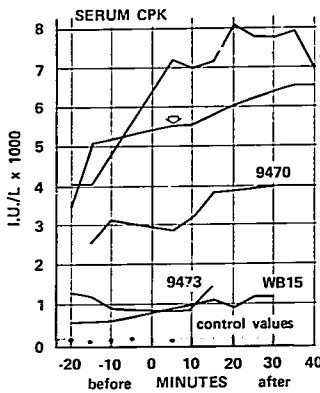


FIG. 8. Serum CPK values after administration of halothane (onset at 20 minutes) to susceptible and nonsusceptible swine. The onset of malignant hyperthermia is indicated by 0 minutes. The range of serum CPK values in nonsusceptible swine is indicated by the shaded area.

References

1. Britt BA, Kalow W: Malignant hyperthermia: A statistical review. Canad Anaesth Soc J 17:293–315, 1970
2. Britt BA, Kalow W: Malignant hyperthermia: Aetiology unknown. Canad Anaesth Soc J 17:316–330, 1970
3. Hall LW, Woolf N, Bradley JWP, *et al.*: Unusual reaction to suxamethonium chloride. Brit Med J 2:1305, 1966
4. Harrison GG, Saunders SJ, Biebuyck JF, *et al.*: Anaesthetic-induced malignant hyperpyrexia and a method for its prediction. Brit J Anaesth 41:844–854, 1969
5. Sybesma W, Eikelenboom G: Malignant hyperthermia syndrome in pigs. Neth J Vet Sci 2:155–160, 1969
6. Allen WM, Berrett S, Harding JDW, *et al.*: Experimentally induced acute stress syndrome in Pietrain pigs. Vet Rec 87:64–68, 1970
7. Woolf N, Hall L, Thorne C, *et al.*: Serum creatine phosphokinase levels in pigs reacting abnormally to halogenated anesthetics. Brit Med J 3:386–387, 1970
8. Allen WM, Berrett S, Harding JDJ, *et al.*: Plasma levels of muscle enzymes in the Pietrain pig in relation to the acute stress syndrome. Vet Rec 87:410–411, 1970
9. Berman MC, Harrison GG, Bull AB, *et al.*: Changes underlying halothane-induced malignant hyperpyrexia in Landrace pigs. Nature 225:653–655, 1970
10. Calbiochem–Stat Pak. Calbiochem Corp., 3625 Medford Street, Los Angeles, California
11. Sigma Chemical Company, 3500 Dekalb Street, St. Louis, Missouri
12. Fiske CH, Subbarrow Y: The colorimetric determination of phosphorus. J Biol Chem 66:375–400, 1925
13. Jaques LB: Determination of the clotting time of whole blood, blood coagulation, hemorrhage and thrombosis. Edited by LM Tocantins and LA Kazal. New York, Grune and Stratton, 1964, pp 29–32
14. Langdell RD, Wagner RH, Brinkhous KM: Determination of the partial thromboplastin time (PTT), blood coagulation, hemorrhage and thrombosis. Edited by LM Tocantins and LA Kazal. New York, Grune and Stratton, 1964, pp 103–107
15. Tocantins LM: Estimation of prothrombin (one-stage method of Quick), blood coagulation, hemorrhage and thrombosis. Edited by LM Tocantins and LA Kazal. New York, Grune and Stratton, 1964, pp 148–150
16. Tocantins LM: Measurement of the rate and extent of clot retraction, blood coagulation, hemorrhage and thrombosis. Edited by LM Tocantins and LA Kazal. New York, Grune and Stratton, 1964, pp 41–44
17. Tocantins LM: Counting platelets in the blood, blood coagulation, hemorrhage and thrombosis. Edited by LM Tocantins and LA Kazal. New York, Grune and Stratton, 1964, pp 44–51
18. Nelson TE, Jones EW, Venable JH, *et al.*: Malignant hyperthermia of Poland China swine: Studies of a myogenic etiology. ANESTHESIOLOGY 35:52–56, 1972
19. Denborough MA, Forster JFA, Hudson MC, *et al.*: Biochemical changes in malignant hyperpyrexia. Lancet 1, #7567:1137–1138, 1970
20. Isaacs H, Barlow MB: Malignant hyperpyrexia during anesthesia: Possible association with subclinical myopathy. Brit Med J 1:275–277, 1970
21. Van den Hende C, Muylle E, Oyaert W: Oxygen utilization and metabolic acidosis after exercise in pigs. Zbl Veterinaermed [A]17, 2:168–173, 1970
22. Anon: Malignant hyperpyrexia. Brit Med J 3:69–70, 1968
23. Thamford NR, Hamelberg WE, Wiederholt WC: Sudden hyperpyrexia during general anesthesia. Surgery 66:850–855, 1969