

Title: SPECTRUM OF MH SUSCEPTIBILITY: DIAGNOSTIC CONTRACTURE PHENOTYPES VS. METABOLIC RESPONSES TO ANESTHETIC CHALLENGE

Authors: T.E. Nelson, Ph.D., E.H. Flewelling, M.D., D.F. Gloyna, M.D.

Affiliation: Department of Anesthesiology, The University of Texas Medical Branch, Galveston, Texas 77550

**Introduction.** Considerable equivocation surrounds the elective and intraoperative diagnosis of malignant hyperthermia (MH). Our experience with elective diagnostic muscle contracture testing in 122 patients has resulted in the distinction of 3 diagnostic contracture phenotypes. Phenotype H muscle has abnormal contracture response to halothane alone, to caffeine alone, and to caffeine plus halothane. It is unequivocal for MH susceptibility. Phenotype K muscle is abnormal for the caffeine plus halothane test. Phenotype N is normal for each of the 3 tests. An unequivocal clinical episode of MH does not exist among our phenotype K patients. For this reason, we sought to produce pigs with the contracture phenotype K and tested for MH susceptibility by an anesthetic challenge protocol.

**Methods.** Five littermate purebred Poland China pigs with contracture phenotype H, five crossbred littermate pigs with contracture phenotype K and five crossbred pigs with contracture phenotype N were used in this study. The diagnostic contracture phenotypes were determined by methods previously described.<sup>1</sup> Each animal was exposed to an anesthetic challenge protocol which was divided into 3 periods: Period I=thiopental induction (20 mg/kg) and maintenance (2.5 mg/kg per 5 min) of anesthesia for 45 min; Period II=thiopental discontinued and halothane, 1.2% end tidal, was administered for 30 min; Period III=halothane continued and succinylcholine, 2 mg/kg bolus dose, was administered 3 times at 20 min intervals between each dose. During the anesthetic challenge period, the following variables were measured:  $V_{O_2}$ ,  $CO_2$  excretion; arterial pressure, gases, pH, and lactate; heart rate; EKG; rectal temperature; end tidal  $CO_2$  and halothane. If MH developed in an animal, minute ventilation was increased to maintain end tidal  $CO_2$  at 4%.

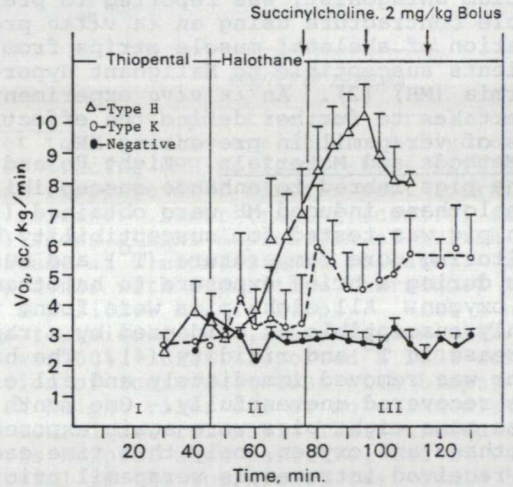
**Results.** During Period I, under thiopental anesthesia, there was no significant difference among pig groups for each variable measured. During Period II,  $V_{O_2}$ ,  $CO_2$  excretion, and lactate increased in the phenotype H and K pigs while no significant change in these variables occurred in phenotype N pigs. The metabolic changes during Period II were greater in phenotype H pigs than for phenotype K pigs. During Period II, 2 of 5 phenotype H pigs had increased  $V_{O_2}$  five times that for Period I, while one phenotype K pig had a  $V_{O_2}$  two times that observed in Period I. During Period III, each of the 5 phenotype H pigs had developed a severe form of the MH syndrome which resulted in death. In phenotype K pigs, a less severe form of MH was observed during Period III. In contrast, blood lactate increased four-fold, while  $V_{O_2}$  and  $CO_2$  excretion increased two-fold during Period III. Except for a decrease in rectal temperature, no significant changes occurred for the variables measured in phenotype N pigs during Period III.

**Discussion.** The potentially significant findings of this study are as follows: (a) the diagnostic contracture phenotype K is an indication of MH

susceptibility in pigs; (b) a relationship exists between diagnostic contracture phenotype and the degree of susceptibility to hypermetabolism during anesthetic-induced MH and the latter supports the hypothesis that (c) a spectrum of MH susceptibility exists among pigs. If applicable to man, these results coupled with the similar varying diagnostic contracture phenotypes observed in man suggest that a similar spectrum of MH susceptibility exists in man. It may be possible that benign forms of MH may occur during anesthesia and go unrecognized in patients who have the potential for developing the more malignant syndrome.

**References.**

- Nelson, TE, Flewelling, EH: Malignant hyperthermia: diagnosis, treatment, and investigations of a skeletal muscle lesion, *Tex Rep Biol Med* 38:105-120 1979.



Effect of an Anesthetic Challenge on Change in  $V_{O_2}$  in Pigs with Varying Susceptibility to Malignant Hyperthermia

Changes in Lactate and Rectal Temperature During Anesthetic Challenge in Pigs with Varying Malignant Hyperthermia Susceptibility

Anesthetic Challenge	Lactate, mmoles/l			Rectal Temp., °C		
	H	K	N	H	K	N
Thiopental	±1.43 (0.70)	1.12 (0.56)	1.51 (0.42)	38.2 (0.61)	38.5 (0.67)	38.3 (0.49)
Halothane	6.56 (8.09)	1.38 (0.66)	1.20 (0.39)	38.1 (0.99)	38.3 (0.91)	37.7 (0.69)
Halothane plus Succinylcholine	18.95 (5.21)	4.60 (2.15)	1.71 (0.47)	40.2 (1.4)	38.4 (0.94)	37.3 (0.60)

\* Values are mean + S.D.; 5 pigs per group. H = Malignant Hyperthermia Susceptible - Contracture Phenotype H; K = Contracture Phenotype K; N = Contracture Phenotype Negative.

Downloaded from http://aesajournal.com/anesthesiology/article-pdf/57/3/A227/629838/000542-198209001-00227.pdf by guest on 20 April 2024