After four months he had no pain and could walk without sticks. Power in his legs had improved, there was increased tone but no clonus, the plantar reflexes were equivocal, and pain, temperature, and vibration were now perceived, though not normally. In June 1974, after 8 months' treatment, the only neurological abnormality was some reduction in vibration sense; a myelogram, however, still showed a block opposite L3. Urinary hydroxyproline excretion had fallen to 2.9 mmol/24 h (380 mg/24 h) and serum alkaline phosphatase to 1610 IU/l.

In October 1974, after 12 months' treatment, pain in the groins recurred, the legs got weaker, and the tendon reflexes were again increased. A month later the pain and weakness were worse, proprioception and vibration sense were absent, and the plantar reflexes were extensor. The dose of calcitonin was doubled to 160 U daily. He continued to deteriorate, ankle clonus reappeared, and Romberg's test became positive again. In January 1975 the dose of calcitonin was increased to 320 U daily. Over the next two months the pain lessened and the signs of spasticity regressed, but signs of posterior column involvement remained prominent. The serum B₁₂ level was normal and the Venereal Disease Research laboratory test was negative. In April 1975 the patient had a myocardial infarct but recovered quickly. He remained free of pain and mobile with the aid of a stick, but he died suddenly in June 1975.

Discussion

The improvement after treatment suggests that calcitonin was responsible. Although relief of pain certainly helped to increase mobility, the improvement in neurological signs was striking. Similar improvement has been reported by Shai *et al.*¹ The mechanism of this response is not clear: reduction in volume of the offending bone and reduction in vascularity are possibilities. The reason for relapse is uncertain; antibodies to calcitonin have been implicated in some patients.² Relapses may be treated by increasing the dose, as in our case, or by using a different calcitonin such as human or salmon.

¹ Shai, F, Baker, R K, and Wallach, S, *Journal of Clinical Investigation*, 1971, **50**, 1927.

² Haddad, J G, jun, and Caldwell, J G, *Journal of Clinical Investigation*, 1972, **51**, 3133.

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Role of hypertension in fulminant hyperthermia-stress syndrome

Since the fulminant hyperthermia-stress syndrome is preceded and accompanied by palpitations and intense peripheral vasoconstriction,¹ hypertension and an increased peripheral resistance probably play a major part in its development. Measurements of blood pressure, cardiac output, peripheral resistance, and peripheral blood flow as the syndrome developed in our third generation susceptible strain of swine showed a significantly higher than normal blood pressure with highly significant haemodynamic changes.

Animals, methods, and results

Animals susceptible to the fulminant hyperthermia-stress syndrome were raised and pretested at the Sinclair Experimental Medicine Research Farm. Their blood pressure was measured via a carotid catheter connected to a pressure transducer and a Hewlett-Packard model 7786A polygraph. Cardiac output was determined with cardio-green by the dye dilution technique via a Hewlett-Packard model 7754A multi-channel analyser. Peripheral blood flow rates were measured with a Satham SP2202 blood flow meter with the detector unit positioned on the femoral artery of the right hind leg. Susceptible animals were premedicated with an equal mixture of sodium thiamylal and pentobarbitone with intravenous thiamylal supplementing nitrous oxide anaesthesia during surgical preparation of the animals. Halo-

thane or succinylcholine, or both, were used as the triggering agent to initiate the syndrome. The data were analysed by programmed calculations with a Hewlett-Packard 9810A calculator. Animal weights ranged from 29.5 to 70.0 kg.

The blood pressure of six susceptible pigs was significantly higher than that of normal pigs. Systolic pressures in susceptible pigs ranged from 160 to 230 mm Hg (mean 185) and diastolic pressures from 115 to 160 mm Hg (mean 135). Normal pigs in the same weight range have a systolic blood pressure of 120 ± 12 mm Hg.² In pig P-16-3 10 minutes after halothane there was a significant reduction in cardiac output, a pronounced rise in blood pressure, a reduction in blood flow through the femoral artery, and a sharp increase in peripheral resistance (see table). The findings in pig P-5-1

Haemodynamic measurements before and after halothane in pigs (P-5-1 and P-16-3) of a strain susceptible to the fulminant hyperthermia-stress syndrome

	Cardiac output (l/min)	Peripheral resistance (kg)	Blood pressure (mm/Hg)	Mean BP (mm/Hg)	Femoral artery	
					flow (ml/min)	resistance (kg)
			<i>P-5-1</i>			
Control	5.5	2.31	200/160	180	146.5	86.0
5 min after halothane	3.8	3.85	240/180	207	95.4	151.9
			<i>P-16-3</i>			
Control	6.57	1.61	230/170	190	172.2	61.18
10 min after halothane	2.25	18.2	280/230	250	147.0	94.3

five minutes after halothane were similar. These results show that an intense peripheral vasoconstriction can occur when a susceptible animal is exposed to halothane.

Discussion

Our previous observations of an intense peripheral vasoconstriction occurring in swine susceptible to the fulminant hyperthermia-porcine stress syndrome,^{1,3} a tenfold increase in rate of metabolism,³ and 30 to 80 times higher rates of substrate cycling^{4,5} led to the hypothesis that the syndrome was caused by an excess activity of noradrenaline.¹ This suggested that concomitantly severe hypertension should develop in our susceptible animals. Indeed, as the syndrome develops the peripheral resistance greatly increases, causing a rise in blood pressure and a decrease in cardiac output.

These haemodynamic changes would increase lactate production and cause lactate and CO₂ to accumulate in blood and tissues. The higher metabolic rate in susceptible animals before the development of the syndrome supports a high rate of heat production. This heat must be dissipated for the animal to maintain thermal balance. The intense peripheral vasoconstriction prevents effective heat loss via the skin and as a result the animal begins to develop hyperthermia. The combination of hypertension, hypermetabolism, and hyperthermia accompanied by an intense peripheral vasoconstriction mediated by noradrenaline makes these animals very susceptible to stress, halothane anaesthesia, or the depolarising action of succinylcholine.

¹ Williams, C H, in *Proceedings of Focus on Malignant Hyperthermia Symposium, Wausau, Wisconsin 1974: Malignant Hyperthermia Syndrome: Current Perspectives and Management*, ed E O Henschel. New York, Appleton-Century-Croft, in press.

² von Engelhart, W, in *Swine in Biomedical Research*, ed L K Burstad, R O McClellan, and M P Burns. Richland, Washington, Pacific Northwest Laboratories, 1965.

³ Williams, C H, Houchins, C, and Shanklin, M D, *British Medical Journal*, 1975, **3**, 411.

⁴ Williams, C H, *et al*, *Proceedings of the American Society of Anaesthesiology*, Abstract, p 199, 11 October 1973.

⁵ Clark, M G, *et al*, *Nature*, 1973, **245**, 99.

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