Gouttas, A., Fessas, P., Tsevrenis, H., and Xefteri, E. (1955). *Sang*, **26**, 911.
Huisman, T. H. J., Wilson, J. B., and Adams, H. R. (1967). *Arch. Biochem.*, **121**, 528.
Huisman, T. H. J., Dozy, A. M., Blunt, M. H., and Hayes, F. A. (1968). *Arch. Biochem.*, **127**, 711.
Kilmartin, J. V., and Clegg, J. B. (1967). *Nature (Lond.)*, **213**, 269.
Lehmann, H., Beale, D., and Boi-Doku, F. S. (1964). *Nature (Lond.)*, **203**, 353.
Lie-Injo Luan Eng, Lie Hong Gie, Ager, J. A. M., and Lehmann, H. (1962). *Brit. J. Haemat.*, **8**, 1.
Perutz, M. F., and Lehmann, H. (1968). *Nature (Lond.)*, **219**, 902.
Perutz, M. F. (1965). *J. molec. Biol.*, **13**, 646.
Perutz, M. F., Kendrew, J. C., and Watson, H. C. (1965). *J. molec. Biol.*, **13**, 669.
Pootrakul, S., Wasi, P., and Na-Nakorn, S. (1967). *Ann. Hum. Genet.*, **31**, 149.
Rigas, D. A., Koler, R. D., and Osgood, E. E. (1955). *Science*, **121**, 372.
Schapira, G., Dreyfus, J. C., and Maleknia, N. (1968). *Biochem. biophys. Res. Commun.*, **32**, 558.
Schroeder, W. A., *et al.* (1968). *Proc. nat. Acad. Sci. (Wash.)*, **60**, 537.
Wasi, P., Na-Nakorn, S., and Suingdumrong, A. (1964). *Nature (Lond.)*, **204**, 907.
Watson, H. C., and Kendrew, J. C. (1961). *Nature (Lond.)*, **190**, 670.
Weatherall, D. (1964). *N.Y. Acad. Sci.*, **119**, 463.

Medical Memoranda

Fulminating Hyperthermia and General Anaesthesia

Brit. med. J., 1968, **4**, 750–751

A paper read by Dr. G. E. S. Relton at the 1967 Belfast meeting of the Association of Anaesthetists stimulated us to look again at the facts of the mysterious deaths of two fit young adults in this region in recent years after minor operations. A number of such occurrences have been published, mainly in Canada (Saidman *et al.*, 1964; Cullen, 1966; Davies and Graves, 1966; Hogg and Renwick, 1966; Lavoie, 1966; Relton *et al.*, 1966; Thut and Davenport, 1966; Purkis *et al.*, 1967; Stephen, 1967), but we know of only one other comparable case so far recorded in the British Isles (Brown, 1954).

Case 1

A 25-year-old man was admitted to hospital in December 1965 after a fall at work. He had sustained a fracture of the right radius at the elbow and a mid-shaft fracture of the left radius. There was nothing of note in the medical history. Physical examination showed a well-built, fit, and muscular young man. Apart from a few abrasions there were no abnormalities other than the injuries mentioned.

He was premedicated with pethidine 100 mg. and atropine 0.6 mg. Anaesthesia was induced with sodium thiopentone 500 mg. followed by suxamethonium 60 mg., and ventilation with 100% O_2, before the passage of a 9.5 cuffed Magill tube. No abnormal response to suxamethonium in the form of increased fasciculation or increased muscular rigidity was noted. Spontaneous respiration returned within a few minutes, and anaesthesia was maintained with nitrous oxide 5 l./min., oxygen 2.5 l./min., and halothane from a Fluotec vaporizer via a Magill circuit.

Closed reduction of the fracture with *x*-ray control was twice attempted but failed. The patient was moved to a theatre for open reduction and fixation. The main operating-theatre formed part of an air-conditioned suite whose air-conditioning was functioning normally.

A tourniquet was applied to the right arm and the operation proceeded. Anaesthesia was not altogether satisfactory. The patient had a persistent tachycardia and a varying respiratory rate. Pethidine 25 mg. intravenously 90 minutes after induction caused transient apnoea, and respiration was "assisted" for four minutes before it was adequate.

As the skin wound was closed, and before plastering, halothane and N_2O was turned off and the patient allowed to breathe pure O_2. At this point the skin was noticed to be "very hot"—a clinical thermometer placed under the tongue registered 110° F. (43.3° C.). Thereafter events moved rapidly, and their sequence is difficult to establish.

All drapes were taken off and cold sponging was begun. At this time extreme rigidity of the skeletal muscles was noted. A second thermometer beneath the tongue registered (by extrapolation) 112° F. (44.4° C.). Two hours had now passed since induction. The patient had become cyanosed and the pulse weak and irregular. Intermittent positive-pressure ventilation with pure oxygen was started by means of a Cyclator. The chest was difficult to inflate, so 30 mg. of tubocurarine chloride was given intravenously, with apparent improvement. While an intravenous saline infusion was being set up the pulse and heart beat disappeared. External cardiac massage was started, and methylamphetamine, dextran, and sodium bicarbonate were given intravenously. One intracardiac injection of adrenaline was given and an external pacemaker tried, but these measures failed to restore the heart beat. The chest was therefore opened, cardiac massage continued, and further intracardiac adrenaline given. Pacemaking by means of direct electrodes was attempted, but despite these measures the heart failed to beat spontaneously. Lack of activity was confirmed by electrocardiography, and death was presumed three hours after induction.

At necropsy both lungs were completely collapsed, and massive collapse of lungs was accepted as the cause of death, though the left lung, at least, could be seen inflating regularly when the chest was opened for cardiac massage. There was no evidence of pulmonary embolism or oedema; the brain showed anoxic changes only, while the heart, kidneys, stomach, and gastrointestinal tract were normal. No specimens of skeletal muscle were examined, nor, regrettably, were blood samples taken during resuscitation for electrolyte and acid–base estimations.

Case 2

This patient, a young woman aged 19, was premedicated with pethidine 50 mg. and atropine 0.6 mg. at 7.45 a.m., before undergoing rhinoplasty. At 8.30 a.m. local application of Brompton cocaine 4 ml. to the nostrils was made, the Moffatt technique being used. Owing to a delay an hour elapsed before induction of anaesthesia was begun, during which time she felt well and her pulse and blood pressure remained within normal limits. At 9.30 a.m. anaesthesia was induced with 2.5% thiopentone 250 mg. and suxamethonium 50 mg. to facilitate oral intubation. Anaesthesia was maintained with 5 litres of N_2O, 2 litres of O_2, and, after spontaneous respiration had returned, by the addition of 2% halothane. During the hour taken to perform the operation the patient's condition was excellent, the pulse rate remaining between 68 and 76, and the blood pressure about 90 mm. Hg systolic. She was in a slight head-up position, and operative conditions were said by the surgeon to be very good.

At 10.30 a.m., at the conclusion of surgery, the tube was removed and the patient conducted to the recovery room; her colour was good and all reflexes were present. At no time during anaesthesia or surgery was there any difficulty with muscle tone or with respiration. There was no abnormal reaction to the induction dose of suxamethonium.

As the patient's level of anaesthesia lightened she started shivering uncontrollably and complained of feeling cold. When the anaesthetist was called to the recovery room to see her the nurse remarked that the skin felt hot. It was observed that she was very flushed. An axillary temperature of 105° F. (40.6° C.) was recorded, and while preparations were made for surface cooling the thermometer was reinserted in the axilla. Within a few seconds cardiac arrest associated with cyanosis and cessation of respiration occurred. At the start of the usual resuscitative measures the thermometer registered 111° F. (43.9° C.) (the mercury was above the top of the

scale). Cardiac massage, ventilation of the lungs with 100% O_2, and surface cooling were continued.

Calcium gluconate 1 g. was injected and sodium bicarbonate 40 mEq infused. After 40 minutes the heart beat returned, in sinus rhythm; 45 g. of urea in invert sugar was injected. Temperature was 107° F. (41.7° C.) at this time, and dropped rapidly to 95° F. (35° C.) with continued cooling. Shivering was uncontrollable, so 50 mg. of suxamethonium was injected intravenously, giving much better control of ventilation. There was no return of consciousness or of spontaneous respiration.

At 12 noon blood gas analysis showed: *p*H 7.01, arterial oxygen saturation 94.5%, P_{CO_2} 36.0, standard HCO_3 7.0, base excess −19. At this time 100 ml. of 8.4% $NaHCO_3$ was infused and a further 1 g. of calcium gluconate given.

At 1 p.m. the blood gas analysis had improved, the only abnormal feature being a base excess of −6. At this time the operation site (previously dry) started to bleed, blood welling from the nose and mouth. The nasopharynx was packed by the surgeon, but continued to ooze steadily. One pint (570 ml.) of uncrossmatched blood was given, and her condition improved a little.

At 1.45 p.m. she was transferred to the intensive care ward for continued ventilation and for routine intensive nursing care. B.P. was low (70/50), pulses were just palpable, and a slightly subnormal temperature (95–96° F.; 35–35.6° C.) was maintained. Aramine 1 mg. was given.

At 2.30 p.m. the haemoglobin was 65%; she was bleeding heavily from the nose and mouth, and needed blood transfusion running constantly. Blood taken for examination showed many defects in the clotting mechanism, presumed to be due to the severe hyperpyrexia.

The patient was unconscious; B.P. 70/50 with peripheral cyanosis. Calcium gluconate 1 g. and hydrocortisone 100 mg. were given. Her temperature was 32° C. The general condition now deteriorated gradually, with widely dilated fixed pupils, mottled cyanosis of the skin, a fall in pulse and blood pressure, and a further drop in temperature, so that artificial warming had to be applied. Death occurred at 10.38 p.m.

At necropsy the lungs were heavy and showed terminal oedema. The intestines contained 1–2 litres of altered blood, otherwise nothing abnormal was seen except the recent operation site.

Discussion

The cases of hyperthermia so far published have a number of basic features in common—namely, high temperature, abnormal muscular rigidity, metabolic acidosis, and cardiovascular collapse, leading rapidly to death. They showed minor variations in the clinical pattern, and the two cases reported here are no exception.

In Case 1 the significance of the tachycardia was not appreciated, and the first awareness of impending or actual hyperthermia in either case was the observation that the patient felt "very hot." In some patients abnormal muscle rigidity has accompanied the use of suxamethonium, but in both the above cases it brought no apparent abnormal response at the time. Muscular hypertonicity was noted in Case 1 after the hyperpyrexia was established, and some two hours after induction, but it is not known how long it had been present. Hypertonicity, however, has also occurred in patients who developed hyperpyrexia and in whom suxamethonium was not administered (Hogg and Renwick, 1966).

The number of possible causes advanced to explain this syndrome gives some indication of how little is known about it. These have been well described in the *Canadian Anaesthetists' Society Journal* (1966) and the *British Medical Journal* (1968).

Of 28 relatives of Case 2, 12 had previously had general anaesthetics without untoward effect. A genetic defect was therefore ruled out.

Treatment.—The outcome in published cases has so far been almost invariably fatal, and it would seem that the patient's only hope of survival depends on early diagnosis and equally prompt treatment. Details of such treatment have been reported (Cullen, 1966; Davies and Graves, 1966; Lavoie, 1966; Stephen, 1967). In one of our cases an injection of tubocurarine chloride appeared to reverse the muscular hyper-rigidity (aided cooling) and allowed the lungs to be ventilated easily. Though it may be possible to cool children relatively rapidly, it is more difficult in adults, and in centres which have the facilities thought might be given to rapid internal cooling via a heat exchanger.

We wish to thank Mr. Mortimer Shaw and Miss P. A. Macleod for permission to report on cases under their care, Dr. W. H. A. Beverley for information about Case 2, and Dr. R. M. H. Anning for advice and help with Case 1.

A. T. Hawthorne, D.A., F.F.A.R.C.S.
M. E. Richardson, M.B., F.F.A.R.C.S.
G. T. Whitfield, M.R.C.S., L.R.C.P., D.A.

The General Infirmary at Leeds.

References

Brit. med. J., 1968, **3**, 69.
Brown, R. C. (1954). *Brit. med. J.*, **2**, 1526.
Canad. Anaesth. Soc. J., 1966, **13**, 45.
Cullen, W. G. (1966). *Canad. Anaesth. Soc. J.*, **13**, 437.
Davies, L. E., and Graves, H. B. (1966). *Canad. Anaesth. Soc. J.*, **13**, 447.
Hogg, S., and Renwick, W. (1966). *Canad. Anaesth. Soc. J.*, **13**, 429.
Lavoie, G. (1966). *Canad. Anaesth. Soc. J.*, **13**, 444.
Purkis, I. E., Horrelt, O., de Young, C. G., Fleming, R. A. P., and Langley, G. R. (1967). *Canad. Anaesth. Soc. J.*, **14**, 183.
Relton, J. E. S., Creighton, R. E., Johnston, A. E., Pelton, D. A., and Conn, A. W. (1966). *Canad. Anaesth. Soc. J.*, **13**, 419.
Saidman, L. J., Havard, E. S., and Eger, E. I. (1964). *J. Amer. med. Ass.*, **190**, 1029.
Stephen, C. R. (1967). *J. Amer. med. Ass.*, **202**, 178.
Thut, W. H., and Davenport, H. T. (1966). *Canad. Anaesth. Soc. J.*, **13**, 425.

Ruptured Abdominal Aorta Infected with Salmonella brandenburg

Brit. med. J., 1968, **4**, 751–752

This report illustrates the difficulty in early diagnosis of salmonella infection of the aorta.

Case Report

A 55-year-old clerk first presented in August 1966 with a three-month history of lassitude and loss of weight. Six years previously he had undergone a partial gastrectomy for chronic gastric ulcer with achlorhydria. On examination he was thin and pale but showed no other abnormal physical signs. Investigations showed: haemaglobin 98%; E.S.R. 10 mm. in one hour; faecal occult blood negative; chest *x*-ray film negative; barium meal examination showed normal postgastrectomy appearances.

He failed to attend for follow-up, but in June 1967 returned complaining of a recurrence of symptoms. There had also been an episode of severe low back pain, worse on the right side, and he had lost a further 5 lb. (2.3 kg.) in weight.

He was admitted to hospital on 9 July. The back pain had almost gone, and he was again noted to be pale and ill but without fever or abnormal physical signs.

Investigations showed: E.S.R. 61 mm.; haemoglobin 91%; W.B.C. 5,500/cu. mm.; urine examination negative; blood urea 27 mg./100 ml.; serum albumin 2.6 g./100 ml.; serum globulin 4.2 g./100 ml.; xylose excretion 4 g. of a 25-g. dose after five hours; faecal fat 24% dry weight; stools negative for occult blood; *x*-ray films of chest and abdomen negative; *x*-ray film of lumbar