Immune response of neonates to oral poliomyelitis vaccine

In the conventional schedule of immunisation infants are given three doses of oral poliomyelitis vaccine starting at, or after, 6 to 8 weeks of age. In the new pulse immunisation strategy three doses of oral poliomyelitis vaccine are given in annual cycles to children under 24 months of age.[1] I carried out a study to see whether a lower age limit could be established in this programme. Neonates were given one dose of oral poliomyelitis vaccine followed by second and third doses at intervals of four weeks. The seroconversion response in the neonates was as good as the response in older infants, indicating that immunisation may be started in the neonatal period.

Patients, methods, and results

I studied 180 neonates and infants with parental consent. The first dose of oral poliomyelitis vaccine was given to groups of 30 infants at 7, 14, 21, 28, 35, and 42 days (± one day) of age. Second and third doses were given at intervals of four weeks. The vaccine was tested and found to be fully potent. At least 30 minutes was allowed between administration of the vaccine and breast feeding. Capillary blood was collected immediately before giving the first dose of the vaccine and four weeks after the last dose. The second sample of blood was collected from only 139 infants.

The paired serum samples were tested together in doubling dilutions from 1/8 to 1/1024 for poliovirus neutralising antibodies as described previously.[2] The second serum sample was collected 12 weeks after the first. As the half life of maternal antibody in the infant's circulation is less than four weeks the persisting maternal antibody titre in the second serum sample would be lower than that in the first by a factor of eight or more. A fourfold or higher titre than the expected residual maternal antibody titre in the second serum sample was taken to indicate the infant's immune response (seroconversion) to the three doses of oral poliomyelitis vaccine.[2,3]

The table shows the frequency of the antibody response in the neonates and infants to three doses of poliomyelitis vaccine according to age at the start of immunisation. It also compares the antibody response of infants aged from 6 to 20 weeks with maternal antibody with that of infants aged from 6 to 51 weeks without maternal antibody from a previous study.[2] The seroconversion response to the three types of poliovirus in infants receiving their first dose during the neonatal period was no less than that in older infants.

Antibody response in neonates and infants to three doses of oral poliomyelitis vaccine according to age at which immunisation was started

Age (weeks)*	n	Seroconversion response (%) to:			Mean seroconversion response (%)
		Type 1	Type 2	Type 3	
1	23	83	83	78	81
2	30	80	90	70	80
3	25	64	96	56	72
4	26	90	95	65	83
5	19	47	68	42	53
6	16	69	81	63	71
1-6	139	73	87	63	75
6-20 (ref 2)	86	72	88	79	80
6-51 (ref 2)	61	66	95	72	78

*Age when first dose of oral poliomyelitis vaccine given.

Comment

As the seroconversion response in infants beginning immunisation from 1 to 4 weeks of age was not less than that in older infants, such neonates may be given oral poliomyelitis vaccine either in the conventional schedule of immunisation or in the pulse immunisation strategy. If the five dose schedule of primary immunisation with poliomyelitis vaccine is followed the first two doses may be given as early as 1 and 5 weeks of age followed by three doses of diphtheria pertussis, and tetanus and oral poliomyelitis vaccine at 9, 13, and 17, weeks.[4] In pulse immunisation the lower age limit for oral poliomyelitis vaccine should be 1 week.

I did not investigate the immune response to oral poliomyelitis vaccine in neonates who were less than 1 week of age. Early investigations on the vaccine showed that there was some inhibition of response in neonates during the first three days of life.[3] The presence of maternal antibody did not seem to inhibit the infant's ability to produce antibodies to the vaccine. Young infants with maternal antibody have recently been immunised with an aerosolised live measles virus vaccine.[5] Though passive immunity inhibits the response to parenteral stimulation by live vaccines, it does not seem to prevent local infection by poliovirus in the gut or by measles virus in the respiratory tract and the consequent active immune response.

I thank Mrs Saroja Christopher for technical help. The centre of virology is supported by the Indian Council of Medical Research, New Delhi.

1 John TJ, Steinhoff MC. Appropriate strategy for immunization of children in India. 3. Community based annual pulse immunization. *Indian J Pediatr* 1981; **48**:677-83.
2 John TJ, Devarajan LV, Luther L, *et al.* Effect of breast-feeding on seroresponse of infants to oral poliovirus vaccination. *Pediatrics* 1976;**57**:47-53.
3 Warren RJ, Lepow ML, Bartsch GE, *et al.* The relationship of maternal antibody, breast feeding and age to the susceptibility of newborn infants to infection with attenuated polioviruses. *Pediatrics* 1964;**34**:4-13.
4 John TJ. Antibody response of infants in tropics to five doses of oral polio vaccine. *Br Med J* 1976;i:812.
5 Sabin AB, Arechiga AF, de Castro JF, *et al.* Successful immunization of children with and without maternal antibody by aerosolized measles vaccine. Different results with undiluted human diploid cell and chick embryo fibroblast vaccines. *JAMA* 1983;**249**:2651-62.

(*Accepted 26 July 1984*)

Indian Council of Medical Research Centre of Virology, Christian Medical College Hospital, Vellore 632 004, India
T JACOB JOHN, FRCPED, PHD, professor and programme director

Survival after prolonged cardiac arrest and accidental hypothermia

Profound accidental hypothermia has been associated with a mortality of up to 80%,[1] but more recent reports indicate much lower mortality provided there is no underlying pathological condition.[2] Successful resuscitation from deep accidental hypothermia and cardiac arrest of several hours' duration has been reported in several patients without any underlying disease.[3] Most of these successful resuscitations have entailed the use of extracorporeal circulation.[3] We report on a patient with accidental hypothermia who was warmed with simpler methods available in most district general hospitals and who survived four hours of cardiac arrest.

Case report

A thin 27 year old unemployed man was admitted deeply unconscious with no detectable cardiac sounds or pulses and gasping intermittently. Ambulancemen reported that he had been sleeping on a park bench overnight; his wife suspected that he had taken some barbiturates after ingesting alcohol. The doctor in the casualty department immediately passed an endotracheal tube, and the cardiac rhythm changed from slow sinus of 48 beats/minute with J waves to ventricular fibrillation. Full cardiac arrest procedure was begun: he was given sodium bicarbonate, lignocaine, direct current cardioversion, adrenaline and calcium infusions, external cardiac massage, and ventilation with 100% oxygen. There was no response.

He was transferred to the intensive therapy unit, where he was ventilated with warmed, humidified oxygen and external cardiac massage was continued. Lower oesophageal temperature was 25°C. Blood samples were taken for estimation of urea, electrolyte, haemoglobin, and barbiturate concentrations and gas tensions; he was given magnesium sulphate 4 g as cerebral protection. Rewarming continued with gastric lavage with warmed fluid, and a warmed intravenous infusion was set up, the rate of infusion being adjusted according to the central venous pressure. These measures were thought necessary because of the contraction of plasma volume that occurs early on in hypothermia and contributes to the hypotension when vasodilatation occurs on rewarming, especially in the presence of heart failure induced by hypothermia.

Core temperature was 31°C four hours later, when defibrillation was successful, and blood pressure was 90/60 mm Hg. In common with other survivors of prolonged cardiac arrest in accidental hypothermia he developed acute pulmonary oedema. This initially responded to simple treatment with diuretics and oxygen, but it recurred and the adult respiratory distress syndrome developed, which together made artificial ventilation necessary for nearly three weeks. Less than a month later, however, he went home fully recovered and with no neurological deficit.

Comment

Alcohol, hypothermia, and barbiturates are known to prolong survival of neurones in circulatory arrest and probably contributed to the survival of this patient.[2] Our main reason for presenting this case, however, is to show that good results may be obtained without resorting to extracorporeal circulation. With simple measures and equipment available in most district general hospitals central re-

warming can be successful. We concur with Althaus that below 27°C life is difficult to detect and the diagnosis obscured,[3] and with Coniam that resuscitation should not be abandoned in a case of hypothermia until the patient has been adequately rewarmed.[4] Disturbing patients with hypothermia may precipitate ventricular fibrillation (as intubation did in this patient). These patients should, therefore, be handled gently and not intubated unless ventilation is inadequate or protective reflexes absent as they were in this case.

1 Freuhan AF. Accidental hypothermia. *Arch Intern Med* 1960;**106**:218-29.
2 White JD. Hypothermia: the Bellevue experience. *Ann Emerg Med* 1979;**8**:417-24.
3 Althaus U, Aeberhard P, Schupach P, Nachbur B, Muhlemann W. Accidental hypothermia. *Ann Surg* 1982;**195**:492-5.
4 Coniam SW. Accidental hypothermia. *Anaesthesia* 1979;**34**:250-6.

(*Accepted 31 July 1984*)

Selly Oak Hospital, Birmingham B29 6JD

L OSBORNE, MB, DA, senior house officer
A S KAMAL EL-DIN, FFARCS, registrar in anaesthetics
J E SMITH, FFARCS, consultant anaesthetist

Correspondence to: Dr L Osborne, Department of Anaesthetics, St Thomas's Hospital, London SE1 7EH.

Is hypokalaemia the cause of paralysis in barium poisoning?

Soluble salts of barium, commonly used industrially, are highly toxic. Weakness and hypokalaemia are the characteristic signs of barium poisoning. Reports have suggested that the weakness is due to hypokalaemia and that potassium is the antidote.[1 2] We describe a patient poisoned by barium in whom the degree of weakness correlated with plasma barium concentrations and not potassium concentrations.

Case report

A 39 year old art teacher attempted suicide by ingesting 40 g barium carbonate, normally used for glazing pottery. She developed colicky abdominal pain, diarrhoea, and vomiting and was admitted to hospital 10 hours after ingestion. On examination she had generalised muscle weakness with active movement against gravity (grade III on the Medical Research Council's grading of muscle power). Her plasma potassium concentration was 1·5 mmol(mEq)/l. After gastric lavage she received sodium sulphate 60 g through a nasogastric tube and magnesium sulphate 2·5 g intravenously. Hypokalaemia was treated with intravenous potassium, 254 mmol in the first three days (see figure).

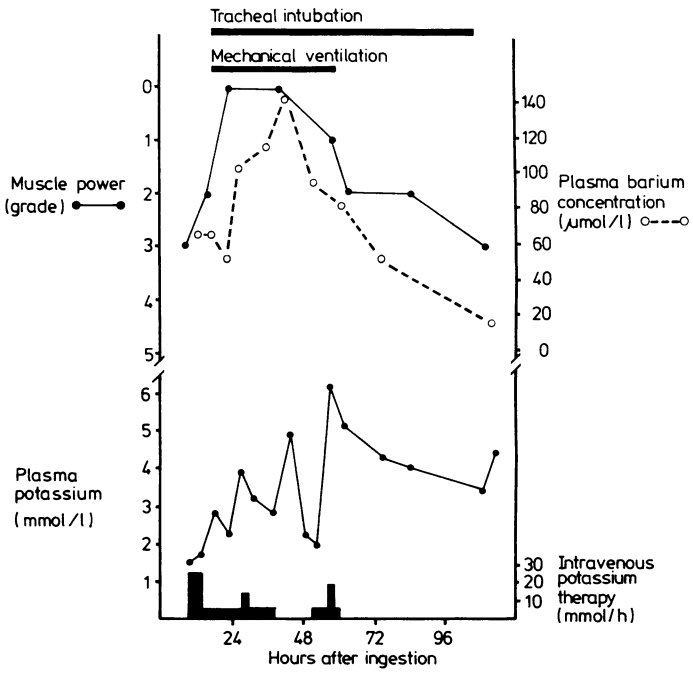
The muscle weakness increased, and 17 hours after ingestion she required mechanical ventilation for respiratory failure. In the next six hours she developed complete flaccid paralysis, which was generalised apart from minimal residual voluntary movement of the eye and eyelid. One day later flickers of muscle activity and weak spontaneous breathing returned. Her vital capacity and cough were adequate to permit extubation four and a half days after ingestion. She had regained normal power a week later. Despite a normal haemodynamic state, from day 2 she showed progressive oliguric renal insufficiency, and three days later her plasma creatinine concentration peaked at 300 μmol/l (3·4 mg/100 ml) (normal 50-1200 μmol/l (0·6-13·6 mg/100 ml)). This resolved within six days.

The figure shows serial plasma barium concentrations (measured by inductively coupled plasma emission spectroscopy), plasma potassium concentrations, and the degree of muscle weakness. Serum magnesium concentration was above normal at 1·3 mmol/l (3·2 mg/100 ml). Electrodiagnostic investigations during the period of flaccid paralysis showed the muscle to be electrically silent and unexcitable. Nerve action potentials were elicited in sensory and mixed peripheral nerves. In the early stages of recovery low amplitude, short duration "myopathic" units were evident and motor conduction velocity was normal. Investigation of peripheral nerve stimulation (using a Myograph 2000) showed no evidence of competitive (non-depolarising) neuromuscular blockade. Biopsy of the vastus medialis muscle showed normal sarcolemmal nuclei, sarcoplasm, and interstitial tissues. Mild and non-specific atrophy (type IIb) was detected on quantitative histochemical examination. The changes characteristic of hypokalaemic paralysis were not present.[3]

Comment

Barium initiates or potentiates synaptic transmission, probably by causing release of acetylcholine.[4] Any ensuing neuromuscular blockade would be expected to be depolarising in nature. Barium also competitively reduces the permeability of cell membranes to potassium, which, again, may lead to membrane depolarisation.[2]

The electrodiagnostic investigation showed that nerve conduction was normal, which suggested that the adverse physiological changes had occurred either in the muscle or at the neuromuscular junction. As the muscle biopsy specimen showed mild and non-specific change the weakness may have been caused primarily by neuromuscular blockade, which, the results of the investigation of nerve stimulation suggested, was probably depolarising in nature.



Relation between muscle weakness, graded according to Medical Research Council's scale, and plasma barium and potassium concentrations.
Conversion: SI to traditional units—Potassium: 1 mmol/l=1 mEq/l. Barium: 1 μmol/l≈5·6 μg/100 ml.

As barium has a depolarising effect on membranes, and as we saw a close correlation between the serial barium concentrations in the patient and the intensity of neuromuscular blockade, we suggest that barium was the direct cause of the muscle weakness. There was no correlation between plasma potassium concentrations and the degree of weakness. The renal insufficiency in this patient may have been due to precipitation of barium sulphate in renal tubules,[5] which suggests that intravenous sulphate—for example, magnesium sulphate—should be avoided in the treatment of barium poisoning.

We thank Dr Vyt Garnys, who performed the barium assays and from whom details of the technique of measurement may be obtained; Drs D Burrows and W J Russell, who advised on the electrodiagnostic studies; Dr P C Blumbergs for the histopathological interpretation; and Ms Angela Roberts for secretarial help.

1 Smith RP, Gosselin RE. Current concepts about the treatment of selected poisonings. *Ann Rev Pharmacol Toxicol* 1976;**16**:189-99.
2 Layzer RB. Periodic paralysis and the sodium potassium pump. *Ann Neurol* 1982; **11**:547-52.
3 Shy GM, Wanko T, Rowley PT, Engel AG. Studies in familial periodic paralysis. *Exp Neurol* 1961;**3**:53-121.
4 Silinski EM. On the role of barium in supporting the asynchronous release of acetylcholine quanta by motor nerve impulses. *J Physiol* 1978;**274**:157-71.
5 Wetherill SF, Guarino MJ, Cox RW. Acute renal failure associated with barium chloride poisoning. *Ann Intern Med* 1981;**95**:187-8.

(*Accepted 5 July 1984*)

Department of Anaesthesia and Intensive Care, Royal Adelaide Hospital, Adelaide 5000, South Australia, Australia

DERMOT M PHELAN, FFARCSI, FFARACS, senior registrar
STEPHEN R HAGLEY, MB, FFARACS, staff specialist

Division of Clinical Chemistry, Institute of Medical and Veterinary Science, Adelaide 5000, South Australia, Australia

MICHAEL D GUERIN, MB, MAACB, registrar

Correspondence to: Dr D M Phelan.