during short-term nitroprusside therapy. Production of infusions during anaesthesia show that thiocyanate concentrations are therefore a poor indication of exposure to cyanide rhodanase. Our studies on patients receiving nitroprusside slow conversion to thiocyanate by the liver enzyme, accumulates mainly in the red cells and there is a relatively In vivo experiments now in progress, suggest a shorter half-life. The hydrogen cyanide cyanide in the molecule (45% of the weight of the sodium (McDowall et al., 1974a,b; Merrifield and Blundell, 1974). The metabolism of nitroprusside is not quite as McDowall and colleagues (1974) suggest. Nitroprusside appears to break down in the blood to release hydrogen cyanide. All the types are carried out under this form of anaesthetic management with a similar absence of neurological sequelae or complications. Therefore it is regrettable that such a valuable method of anaesthetic practice would find itself in jeopardy for lack of suitable drugs. It is to be earnestly hoped that pharmaceutical companies will be able (and willing) to continue to supply us with suitable drugs so that spinal anaesthesia will be available to all patients who may derive the benefits as outlined in your Editorial.

Z. LETT
Hong Kong

REFERENCES

SPINAL ANAESTHESIA

Sir,—Your informative Editorial of April, 1975, on the above subject is of great importance to all anaesthetists in general and particularly to those who, like you, believe that spinal anaesthesia should have a place in our armamentarium.

It is enlightening to see confirmation that various groups of workers such as Dripps and Vandam (1954) in 10,998 cases, Moore and Bridenbaugh (1968) in 12,386 cases and Noble and Murray (1971) in 78,746 cases of spinal anaesthesia did not find evidence of permanent neurological deficits.

As has been reported earlier from here (Lett, 1964, 1967, 1969), a considerable number of operations of various types are carried out under this form of anaesthetic management with a similar absence of neurological sequelae or complications.

Therefore it is regrettable that such a valuable method of anaesthetic practice would find itself in jeopardy for lack of suitable drugs. It is to be earnestly hoped that pharmaceutical companies will be able (and willing) to continue to supply us with suitable drugs so that spinal anaesthesia will be available to all patients who may derive the benefits as outlined in your Editorial.

Z. LETT
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REFERENCES

SPINAL ANAESTHESIA

Sir,—The increasing interest in the use of sodium nitroprusside to induce hypotension during anaesthesia prompts us to comment on recent communications to this journal (McDowall et al., 1974a,b; Merrifield and Blundell, 1974).

The metabolism of nitroprusside is not quite as McDowall and colleagues (1974) suggest. Nitroprusside appears to break down in the blood to release hydrogen cyanide. All the cyanide in the molecule (45% of the weight of the sodium nitroprusside) is set free. In vitro, 50% of the cyanide is liberated within 20 min. In vivo experiments now in progress, suggest a shorter half-life. The hydrogen cyanide accumulates mainly in the red cells and there is a relatively slow conversion to thiocyanate by the liver enzyme, rhodanase. Our studies on patients receiving nitroprusside infusions during anaesthesia show that thiocyanate concentrations increase by only a small amount, or may even decrease (Vesey et al., 1974). Plasma thiocyanate concentrations are therefore a poor indication of exposure to cyanide during short-term nitroprusside therapy. Production of cyanide from the thiocyanate by "thiocyanate oxidase" will contribute a negligible amount compared with that released from the nitroprusside. Boxer and Rickards (1952) demonstrated that the equilibrium ratio of thiocyanate: cyanide in body fluids is normally 1000:1.

The total quantity of nitroprusside infused appears to be less critical than the rate of infusion of the substance since the supply of thiocyanate limits the body's ability to detoxicate cyanide. Two of our patients received 424 mg and 2,777 mg of sodium nitroprusside respectively over a prolonged period (Vesey et al., 1974). In the second case the red cell cyanide concentration increased to 0.8 mg%, a value greater than that for whole blood cyanide reported for a case of cyanide poisoning by Ansell and Lewis (1970). The lethal dose of hydrogen cyanide by mouth is about 100 mg, although some suggest that it is nearer 50 or 60 mg (Gettler and Baine, 1938; Sollman, 1957). Introduced directly into the blood, it is certainly less than 50 mg. Thus 750 mg, as used by Merrifield and Blundell (1974) would release at least six times the fatal dose of hydrogen cyanide within a period of as many hours and it is probable that detoxication mechanisms were overwhelmed.

It is our suggestion that, since cyanide is released at a relatively slow rate from nitroprusside and thus accumulates mostly in the erythrocytes, the normal histotoxic manifestations may be delayed and in addition more subtle effects on oxygen transport may develop. A large dose of hydroxocobalamin (Vesey et al., 1974) to which thiosulphate (which appears to act synergistically with vitamin B12, Delga, 1965) may be added, following or during nitroprusside infusion, might avoid the consequences reported by Merrifield and Blundell (1974). Since the ability to detoxicate cyanide may be reduced in certain patients such as those with liver disease, or Leber's optic atrophy, and exposure to cyanide might prove damaging to those with nutritional deficiency or faulty absorption of vitamin B12, individuals should not receive nitroprusside (Wilson, Vesey and Cole, 1971; Vesey et al., 1974).

Hypothermia appears to be a further complication of this technique (Merrifield and Blundell, 1974). It has not been observed in our patients, who were given much lower rates of infusion, but it would not be an unexpected effect of both the peripheral vasodilatation and the inhibition of the cellular respiration by the cyanide released from the nitroprusside. It has been noted in mice receiving nitroprusside 5 mg (Burke and Mann, 1970), a dose lower than the total dose used by Merrifield and Blundell (1974).

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REFERENCES
Sir,—Thank you for giving us an opportunity to comment on the letter received from Drs Vesey and Cole.

We were delighted to see that their work explains the slow and progressive development of the toxic signs of nitroprusside overdose. Of course we agree that it is the rate of infusion and not a total dose which is important, and indeed quoted our results in terms of dose per hour. We seem to be in agreement also that hydroxocobalamin might act clinically as an effective cyanide antagonist.

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N. P. Keaney
J. M. Turner
J. R. Lane
Y. Okuda

ON THE CIRCULATORY AND TOXIC EFFECTS OF SODIUM NITROPRUSSIDE

Sir,—Apparently, some confusion surrounds the relative importance of arterial pressure and blood flow in the successful use of deliberate hypotensive techniques. Induced hypotension is utilized for one of two aims: (1) facilitation of vessel surgery (such as intracranial aneurysms and coarctation of the aorta), and (2) reduction of blood loss (such as radical neck operations). Hypotension may facilitate vessel surgery without a reduction in cardiac output being necessary. Under these circumstances it is the decrease in vessel tension and not the decrease in blood flow that is desirable. Hypotensive drugs which provide minute-to-minute control of arterial pressure, such as nitroprusside or trimetaphan, administered in an intravenous infusion, would then be most useful. However, the success of induced hypotension in producing a relatively bloodless operative field depends on reduction of the cardiac output (or the blood flow at the operative site). This has been shown clearly by Didier, Clagett and Theye (1965).

It has been demonstrated that the increase in cardiac output with nitroprusside is related to the increase in heart rate (Wildsmith et al., 1973; Styles, Coleman and Leary, 1973). One may seriously question the success and safety of such a technique in reducing the amount of bleeding. Tachycardia during induced hypotension may result in increased oozing as a result of repetitive spike filling of the vessels (Larson, 1964), and may ultimately lead to failure of the technique (Larson, 1964; Hellewell and Potts, 1966; Salem and Ivankovic, 1970). If sodium nitroprusside is used, this may result in the administration of a large and toxic dose of the drug. This is likely to occur in children who are known to be resistant to the induction of hypotension (Anderson, 1955; Salem et al., 1974). Increasing the rate of infusion is not the answer to the problem, but with beta-adrenergic blockade the total dose of nitroprusside may be kept to a minimum, thus avoiding catastrophes similar to the case reported by Merrifield and Blundell (1974).

It must be emphasized that acidosis is not a feature of induced hypotension when other drugs are used, provided that adequate oxygenation is maintained and the value of arterial $P_{O_2}$ is within normal limits. On the other hand, the acidosis seen with large doses of nitroprusside results from depressed oxygen uptake as a result of its conversion to thiocyanate and subsequent oxidation to cyanide (McDowall et al., 1974). This was observed by Dr Paul Boyan, 20 years ago, but has now been published.

For these reasons, nitroprusside seems to be a poor choice in long operations in which reduction of bleeding is desirable. In contrast, pentolium appears to offer advantages. The use of nitroprusside should be restricted to procedures where minute-to-minute control of pressure is desirable for a short period.

M. R. Salem
F. Y. Dalal

REFERENCES


ANAPHYLACTIC REACTIONS INDUCED BY INFUSION OF POLYGELINE (HAEMAGGEL)

Sir,—We read with interest the report of Lund (1973) concerning a case of anaphylactic reaction to polygeline (Haemagel). It was our practice to infuse polygeline if the arterial pressure decreased during and after induction of anaesthesia, but following anaphylactic reactions to polygeline in eight patients, this practice has stopped.

The first patient was a 40-year-old healthy man who was scheduled for lumbar laminectomy. There was no history of allergy. The arterial pressure was 120/70 mm Hg before operation. Following induction of anaesthesia by the i.v. injection of a barbiturate (enbominal—a short acting barbiturate differing from thiopentone only by substitution of N for the S atom), tracheal intubation was performed with the aid of suxamethonium i.v. and anaesthesia was maintained with nitrous oxide in oxygen, halothane and gallamine. The patient was turned to the prone position. Shortly afterwards the arterial pressure decreased to 100/80 mm Hg.