

compared those used by the Hospital for Sick Children, Great Ormond Street, Birmingham Children's Hospital, and the Brompton Hospital. All three schedules agree fairly closely on doses for children over 2 years, but under this age there are many discrepancies. It is generally accepted that the younger the child, the greater his tolerance to digoxin, except in the neonatal period when intoxication to many drugs is common because of inadequate renal function and poorly developed enzyme systems.

At any age, there is only a small margin between the effective dose and toxicity of digoxin. With the introduction of radioimmunoassay for plasma digoxin concentrations, it should be possible to assess the safe therapeutic dose for children. Using this method, adult therapeutic concentrations have been shown by Chamberlain, White, Howard & Smith (1970) to lie between 0.5 ng and 3 ng/ml plasma (mean 1.6 ng).

Plasma digoxin concentrations have been measured in more than thirty children, aged 1 week to 10 years, from the Royal Alexandra Hospital, Brighton, and the Hammersmith Hospital. They were all well digitalized for control of heart failure due to a variety of congenital heart disorders. The Brompton Hospital dosage schedule used was:

Under 4 weeks	0.01 mg (digoxin/kg body wt)/day
4 weeks–2 years	0.02 „ ( „ „ „ „ ) „
Over 2 years	0.01 „ ( „ „ „ „ ) „

Plasma digoxin concentrations 6–8 h after an oral maintenance dose, were measured by radioimmunoassay. In most cases, results fell between 1 and 2 ng/ml plasma (average 1.4 ng), agreeing well with therapeutic adult plasma concentrations. No toxic symptoms were noted and heart rate and signs of failure were well controlled.

The Brompton Hospital dosage (after Nadas, 1966) has, therefore, proved satisfactory and safe in our series of children.

#### REFERENCES

- CHAMBERLAIN, D. A., WHITE, R. J., HOWARD, M. R. & SMITH, T. W. (1970). Plasma digoxin concentrations in patients with atrial fibrillation. *Br. med. J.*, 3, 429.  
 NADAS, A. S. (1966). *Paediatric Cardiology*, 2nd ed., p. 783. London: W. B. Sanders & Co.

#### Action of prostaglandins A<sub>2</sub>, B<sub>1</sub>, E<sub>2</sub> and F<sub>2α</sub> on superficial hand veins of man

J. G. COLLIER, S. M. M. KARIM, B. ROBINSON\* and K. SOMERS

*Medical Unit, St. George's Hospital, London SW1, and Departments of Pharmacology and Medicine, Makerere University, Kampala, Uganda*

The action of prostaglandins (PGs) on superficial hand veins was studied using a modified version of the technique previously described (Nachev, Collier & Robinson, 1971). The distensibility of the vein at a standard congesting pressure was measured by means of a light weight lever, one end of which rested on the skin over the summit of the vein, while the other moved over a millimetre scale. The lever was arranged so that vertical movement of the vein was magnified 2.5 times. Prostaglandins in saline solution were infused into the vein at 0.25 ml/min and the response to each dose was measured at the 6th, 11th and 15th min of infusion. The action of each prostaglandin was investigated both in resting veins, and in veins precontracted

by a continuous local infusion of either noradrenaline or 5-hydroxytryptamine (Collier, Nachev & Robinson, 1970).

PGB<sub>1</sub> caused venoconstriction when infused over the dose range 100–500 ng/min in three experiments; doses below the constrictor range had no dilator effect when infused into veins precontracted with noradrenaline (2 expts.). PGF<sub>2α</sub> caused venoconstriction over the dose range 20–500 ng/min in four experiments; subconstrictor doses had no dilator effect (two expts.).

PGA<sub>2</sub> and PGE<sub>2</sub> had no action on resting veins, but caused vasodilation of veins which had been precontracted with either noradrenaline or 5-hydroxytryptamine. PGA<sub>2</sub> had a dilator effect over the range 20–400 ng/min in five experiments. PGE<sub>2</sub>, at an infusion rate of 100 pg/min, had a marked venodilator effect in all of six experiments; maximum dilatation was usually achieved at a rate of 1 ng/minute. After infusions of PGE<sub>2</sub> at rates of 10 ng/min or more a flare developed in the skin over the veins draining the infusion site. The flare lasted for up to 2 h, and after doses of 100 ng/min was accompanied by burning pain.

Venodilatation in response to PGE<sub>1</sub> and PGA<sub>1</sub>, and constriction to PGF<sub>2α</sub> has previously been reported in dogs (Greenberg & Sparks, 1969; Hedwall, Abdel-Sayed, Schmid & Abboud, 1970; and Mark, Schmid, Eckstein & Wendling, 1971). The observation that PGB<sub>1</sub> and PGF<sub>2α</sub> constrict the circular muscle of human superficial veins while PGA<sub>2</sub> and PGE<sub>2</sub> cause dilatation provides further evidence that there may be more than one receptor for prostaglandins in a single tissue. Contrary actions of prostaglandins have previously been noted in circular muscle of the gut of man and guinea-pig (Bennett & Posner, 1971), and in circular muscle of human bronchi (Sweatman & Collier, 1968). The development of pain after intravenous PGE<sub>2</sub> has not previously been reported.

#### REFERENCES

- BENNETT, A. & POSNER, J. (1971). Studies on prostaglandin antagonists. *Br. J. Pharmac.*, **42**, 584–594.
- COLLIER, J. G., NACHEV, C. & ROBINSON, B. (1970). A new method for studying the pharmacology of the superficial veins in conscious man. *Br. J. Pharmac.*, **40**, 574P.
- GREENBERG, R. A. & SPARKS, H. V. (1969). Prostaglandins and consecutive vascular segments of the canine hindlimb. *Am. J. Physiol.*, **216**, 567–571.
- HEDWALL, P. R., ABDEL-SAYED, W. A., SCHMID, P. G. & ABOUD, F. M. (1970). Inhibition of venoconstrictor responses by Prostaglandin E<sub>1</sub>. *Proc. Soc. exp. Bio. Med.*, **135**, 757–759.
- MARK, A. L., SCHMID, P. G., ECKSTEIN, J. W. & WENDLING, M. G. (1971). Venous responses to prostaglandin F<sub>22</sub>. *Am. J. Physiol.*, **220**, 222–226.
- NACHEV, C., COLLIER, J. G. & ROBINSON, B. F. (1971). A simplified method for measuring compliance of superficial veins. *Cardiovasc. Res.*, **5**, 147–156.
- SWEATMAN, W. J. F. & COLLIER, H. O. J. (1968). Effects of prostaglandins on human bronchial muscle. *Nature, Lond.*, **217**, 69.

#### Biphasic response of limb blood flow to intravenous methoxamine in anaesthetized man

G. J. J. FUZZEY, C. E. HOPE\* and J. P. PAYNE

*Research Department of Anaesthetics, Royal College of Surgeons of England, and St. Peter's Hospitals, London*

A biphasic response of limb blood flow to intravenous methoxamine was observed in four patients during nitrous oxide-oxygen-halothane anaesthesia. The details of the anaesthetic and experimental methods have been described previously (Fuzzey, Hope & Payne, 1971).

The four patients (ages 46–70 years) developed hypotension with a mean blood pressure of 44 mmHg and a mean heart rate of 66/minute. Forty seconds after the