CONTROLLED HYPOTENSION WITH ARFONAD IN PAEDIATRIC SURGERY

BY

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Since the methonium compounds were first used to lower the blood pressure during surgery (Organe, 1950; Davison, 1950; Enderby, 1950; Shackleton, 1951) a fairly extensive literature has accumulated on controlled hypotension. The effects of other ganglion-blocking agents have been reported, the last being pentolinium tartrate (Enderby, 1954). The short-acting agent "arfonad" was first reported in American literature by Nicholson *et al.* (1953) and Sadove *et al.* (1953), and in this country by Magill *et al.* (1953), Anderson and McKissock (1953), Scurr and Wyman (1954), and Kilduff (1954). In some of these papers the mode of action of arfonad and its advantages over other ganglion-blocking drugs are described, and are therefore not repeated.

In previous literature it has been shown that, weight for weight, children are more tolerant of the depressant and the relaxant drugs used by anaesthetists than are adults (Anderson, 1951). The purpose of this paper is to show that children are also tolerant of the drugs used to produce hypotension, and that the technique of controlled hypotension can be used in the surgery of children with no greater danger than in adults.

Reports on the use of the hypotensive drugs have so far been concerned mainly with adults. Of the 250 cases reported by Scurr and Wyman, only two were under 10 years of age. Kilduff includes three children under 10 in his series of 10 cases. These authors stressed the resistance shown by young adults to the ganglion-blocking agents. This paper stresses the resistance shown by children. Although the present series is small (44 children in 18 months), it is thought that it provides enough information for certain conclusions to be reached. The reason why there are not more cases is the obvious one: there are not many occasions when both the surgeon and the anaesthetist are confident that the hazards of using the hypotensive technique are more than outweighed by the surgical risk without it. But in neurosurgery and in certain cases requiring careful plastic reconstruction the use of controlled hypotension has proved invaluable. Of the 44 children 29 were under 7 years old (Table I).

TABLE I.—Analysis of 44 Cases

Age in Years	Type of Surgery		
	Neurosurgery	Genito-urinary	General
5/12		1	
8/12		1	
11/12		1	
1	2	3	
2	3	1	
3	4	1	
4			1
5	2	1	2
6	4		2
7	3		
8	2		
9	1	1	
10	2		
11	2	1	1
12	1	1	
	26	12	6

Technique

I believe that arfonad delivered by drip transfusion is the method of choice for inducing hypotension in children, because of the great flexibility of control so obtained. That arfonad needs to be administered by drip transfusion seldom proves to be a disadvantage in practice, for paediatric surgery which demands controlled hypotension also requires, as a rule, a cut-down drip transfusion for replacing blood loss. The methonium compounds were used before supplies of arfonad were made available for trial, but the results were not satisfactory. The child, like the young adult, proved very resistant to these drugs, with the result that when hypotension was produced it lasted for so short a time that repeat doses were often needed. These repeat doses produced tachyphylaxis, so that procainamide was added in an attempt to keep the blood pressure down to the required level.

The first important observation to be made was any change in the systolic blood-pressure reading after the table had been tilted. This was often a useful guide to the patient's reaction to arfonad. The drip was run slowly at first, for it was found easier to control the blood pressure if this was allowed to fall gradually from the beginning.

Strength of Solution

So variable is individual reaction to these drugs that it has proved difficult to find the most suitable strength of solution. That used for adults is usually 0.1% (1 mg. per ml.). The tendency early in this series was to use too weak a solution. This carried the risk of overloading the child with fluid in order to keep the pressure down to the required level. For example, Case 14 (a child of 6) required a drip rate of 160 in order to keep the pressure between 60 and 70 mm. Hg systolic (Table II). The strength of the solution was then doubled to 0.2% (2 mg. per ml.), when this blood-pressure level could be maintained at a drip rate of between 8 and 16 drops a minute. Case 12 (also a child aged 6) required a triple-strength solution 0.3% (3 mg. per ml.) to keep the systolic blood pressure between 60 and 70 mm. Hg with a drip rate varying between 14 and 20 drops a minute.

The present practice is to use the 0.1% solution of arfonad for infants and children up to 5 years old. A double-

TABLE II

Case No.	Age in Years	Operation	Operating Time (Minutes)	Total Arfonad Used (mg.)	Strength of Solution (mg./ml.)	Drip Rate (Drops/min.)
1	5/12	For ectopic bladder	90	10	1.0	8-16
2	8/12	"	110	80	0.5	12-58
3	11/12	Cystectomy	130	45	1.0	5-10
4	1	For ectopic bladder	100	55	0.5	20-30
5	2	Craniotomy	50	190	1.0	53 (average)
6	2	"	60	50	0.5	28
7	2	For "ectopic bladder	120	270	2.0	12-48
8	3	"	45	5	0.5	10
9	3	Craniotomy	50	90	1.0	40
10	3	"	90	25	1.0	8-32
11	5	"	75	50	1.0	3-40
12	6	Recto-sigmoidectomy	120	222	3.0	14-20
13	6	Craniotomy	90	14	1.0	16-48
14	6	"	130	280	1.0	30-140
15	6	"	75	140	2.0	8-16
16	7	"	100	25	1.0	10-80
17	7	"	40	21	2.0	16-20
18	7	"	70	220	2.0	8
19	8	"	35	120	1.0	24-44
20	9	"	60	500	2.0	30-50
21	11	"	210	250	1.0	70 (average)
22	11	Plastic to genitalia	60	250	1.0	10
23	11	Craniotomy	50	90	1.0	40-60
24	12	Plastic to urethra	150	250	2.0	12-48
25	12	Craniotomy	120	160	1.0	20-40
						28 (average)
						6-60

Full data were recorded in only 25 out of the 44 cases.

strength solution, 0.2%, is given to children of 6 years and upwards. The strength of the solution is increased still further if hypotension can be maintained only with an excessive drip rate.

Results

Satisfactory hypotension was produced together with improved operating conditions in every case.

Five of the first 20 cases received procainamide because a suitably low blood pressure could be maintained only with an excessive drip rate. Since the use of stronger solutions of arfonad (in 24 cases) procainamide has not been given.

There was no operative death in the series. One child, aged 4 (who had thyroidectomy for thyrotoxicosis), died within 24 hours of operation from acute heart failure, having been extremely well post-operatively, and talking to a nurse a few minutes before her death. One of the infants caused temporary alarm during the operation when the pulse became imperceptible owing to the drip being accidentally accelerated.

Blood loss was replaced whenever considered necessary (three cases).

In only two cases was a vasopressor drug used; this was given to raise the blood pressure quickly to identify and control bleeding-points before closing the dura mater. In all the other cases the blood pressure returned to near normal levels within a few minutes of stopping the arfonad and levelling the table.

Summary

A series of 44 children is presented in which surgery was performed under controlled hypotension induced by arfonad. An analysis of these cases is shown in tables.

It is concluded that controlled hypotension can be used in paediatric surgery, when indicated, with no greater danger than in adult surgery.

The tolerance of the child raises certain problems in technique of administration, which are described.

The value of the flexibility of action of arfonad when given by drip transfusion is emphasized.

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REFERENCES

- Anderson, S. M. (1951). *Lancet*, 2, 965.
— and McKissock, W. (1953). *Ibid.*, 2, 754.
Davison, M. H. A. (1950). *Ibid.*, 1, 252.
Enderby, G. E. H. (1950). *Ibid.*, 1, 1145.
— (1954). *Ibid.*, 2, 1097.
Kilduff, C. J. (1954). *Ibid.*, 1, 337.
Magill, I. W., Scurr, C. F., and Wyman, J. B. (1953). *Ibid.*, 1, 219.
Nicholson, M. J., Sarnoff, S. J., and Crehan, J. P. (1953). *Anesthesiology*, 14, 215.
Organe, G. (1950). *Proc. roy. Soc. Med.*, 43, 181.
Sadove, M. S., Wyant, G. M., and Gleave, G. (1953). *Anaesthesia*, 8, 175.
Scurr, C. F., and Wyman, J. B. (1954). *Lancet*, 1, 338.
Shackleton, R. P. W. (1951). *British Medical Journal*, 1, 1054.

It was a hundred years ago that JOHN SNOW, well known as an anaesthetist, asserted that a cholera epidemic raging in London would cease if the handle of a pump in Broad Street (now Broadwick Street), Soho, were removed. He was gathering evidence that cholera is a water-borne disease, and found that all the infected persons in this epidemic had drawn water from the Broad Street pump. The epidemic, which had caused 500 deaths in 10 days, stopped immediately the pump was put out of action. Hard by where the pump once stood is now a public house, and, in response to a request that this landmark in epidemiology should be commemorated, the owners, Messrs. Watney, Combe, Reid and Co., agreed to change its name from the "Newcastle On Tyne" to the "John Snow." The occasion was celebrated on July 5 when Professor BRADFORD HILL, F.R.S., before a gathering of epidemiologists, recalled these events and unveiled the new inn sign depicting John Snow. Some mementoes of Snow are now on permanent view at the premises.

THE POTENTIATION OF BARBITURATE ANAESTHESIA BY DINITRO-*O*-CRESOL

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Our attention was recently drawn to the findings of Bain (1952) and Brody and Bain (1954) that a wide range of barbiturate drugs exhibit *in vitro* dissociating effects on oxidative and phosphorylating processes in liver and brain mitochondria, qualitatively similar to, although quantitatively less than, those produced by dinitrophenol (D.N.P.). Bain also stated in a footnote that barbiturate anaesthesia in rats and mice was potentiated by dinitrophenol, while Brody and Bain showed that the effects of thiobarbiturates on mitochondrial preparations more closely resembled those of D.N.P. than did those of oxygen barbiturates.

The widely used agricultural herbicides dinitro-*ortho*-cresol (D.N.C.) and dinitro-*sec*-butylphenol (D.N.B.P., "dinoseb") have a mode of toxic action almost indistinguishable from that of D.N.P., and are sufficiently hazardous in agricultural usage to present a distinct possibility of occupational poisoning. Sedation by oral or parenteral barbiturates has hitherto been advised to allay any dangerous restlessness or excitement which may occur in such cases (Bidstrup and Payne, 1951; B.M.A., 1951; Martindale, 1952; Edson, 1955). There also exists the possibility that a case of mild or even severe D.N.C. intoxication may require the induction of surgical anaesthesia for some essential operative procedure, such as the treatment of physical injuries. A series of experiments has therefore been carried out to compare the responses of normal and D.N.C.-poisoned animals to the narcotic effects of six representative barbiturates.

Materials and Methods

The animals used were adult male and female albino rats of Glaxo-Wistar strain, acclimatized to our laboratory conditions (67–76° F. (19.5–24.5° C.) during the experimental period) and maintained on M.R.C. Diet No. 41. D.N.C. was administered intraperitoneally as a 1% solution of the sodium salt, the dose mainly used (17–20 mg./kg.) being that known from previous work to cause moderate to severe D.N.C. poisoning with an expected 20–30% mortality, under our experimental conditions. (In order to maintain a direct check on this point, a "D.N.C. control group" was included in all but one of the trials. The mortality in these 48 animals was 29%.)

The oxygen barbiturates investigated were pentobarbitone ("nembutal," intraperitoneally), hexobarbitone ("cyclonal," intravenously), amylobarbitone ("amytal," i.v.), and phenobarbitone ("gardenal," i.v.), the thiobarbiturates being thio-pentone ("pentothal," i.v.), and thialbarbitone ("kemithal," i.v.). All were administered as freshly prepared solutions of the sodium salts, injections being carried out by one person, with due care to avoid any marked variation in the speed of injection into individual animals and in the experimental groups.

Preliminary trials with each barbiturate indicated the dosage likely to cause a degree of narcosis with a readily recognizable onset and duration. A state of deep flaccid "surgical" anaesthesia was sought in most trials, since