THE REDUCTION OF SURGICAL HAEMORRHAGE

SOME OBSERVATIONS ON CONTROLLED HYPOTENSION WITH METHONIUM COMPOUNDS

BY

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The literature of the methonium compounds has grown considerably during the past two years. The pharmacology and the physiological action of the group have been fully discussed by Paton and Zaimis (1948, 1949). Decamethonium as a relaxant was introduced by Organe in 1949. Other publications have followed, notably one by Hunter in October, 1950. The hypotensive action of the "middle" numbers of the group, first indicated by Organe when studying pentamethonium as an antidote to decamethonium, has been exploited by several workers in the treatment of hypertension (Campbell and Robertson, 1950; Turner, 1950; Saville, 1950). The action of hexamethonium on gastric secretion has been reported upon by Kay and Smith (1950), as well as by other workers. Armstrong Davison (1950) and Enderby (1950) have reported on the use of drugs of the group to produce hypotension during surgery in order to obtain reduced bleeding.

It is my belief that many anaesthetists are now using the methonium compounds for this last purpose, and I feel that many of us are working in ignorance of the experience and results of our colleagues. Since Enderby and I demonstrated the technique of producing hypotension during an operation at a meeting of the Society of Anaesthetists of the South-west Metropolitan Hospital Region at Winchester in May, 1950, we have received many inquiries about the technique and the use of the methonium drugs. This correspondence suggests that many anaesthetists may be groping along the dark passages already traversed by those of us who have been using the technique for some time. I do not claim to have reached daylight myself as yet, but in the hope that the results of my experience, and those of my colleagues in the plastic unit, may be helpful to others, and stimulate research into what may prove a useful field of activity, I venture to record certain clinical impressions that I have gained during a year's growing familiarity with the use of the methonium compounds to reduce surgical bleeding.

The idea of lowering the blood pressure during surgery, and so reduce bleeding, was introduced to us in this country by Griffiths and Gillies in 1948, and further amplified by Gillies in his Clover Lectures to the Faculty of Anaesthetists in 1950. These workers in Edinburgh achieved hypotension by using the total spinal technique. By this technique they have shown that considerable falls in blood pressure may be produced by spinal block high enough to paralyse the thoracic sympathetic. They also showed that an adequate circulation can be maintained with considerable hypotension present (60 mm. of Hg, for instance), given full oxygenation and vasodilatation. After examining the results of investigations of the action of tetraethylammonium chloride, and the two methonium compounds, hexamethonium and pentamethonium, Enderby suggested to us at the Plastic Unit

at Rooksdow House that these drugs might be used as an alternative to the total spinal technique. It must be realized that the autonomic ganglion block produced by these drugs is unselective, and that a combined sympathetic and parasympathetic paralysis is obtained. It was quickly realized that the effect was considerably influenced by the position of the patient, and that the hypotension produced was partly postural.

Choice of Drug

Previous work having shown that pentamethonium was slightly more effective in producing hypotension than the tetraethylammonium, it was with the methonium compound that we began to work. For fully three-quarters of the cases done by me personally, pentamethonium iodide has been used. Latterly hexamethonium bromide has become the drug of choice, it being my impression that this member of the group is slightly more certain in its action. It has been suggested by one of my colleagues that the hypotensive action of pentamethonium is enhanced if decamethonium has been used for relaxation during intubation or early in the anaesthetic; I have no personal experience of this combination.

Dosage.—In the early days small initial doses were the rule, 10 mg., followed by another 10 or 20 mg. after a period of observation, being used; but as time went on, and our confidence grew, we increased the initial dose, finding much greater certainty with no added worries, until I now regularly employ 50 mg. initially for a healthy adult. Additional dosage to maintain hypotension is dictated solely by circumstances and no hard-and-fast rules can be laid down. If the pressure rises to 75 or 80 mm. half the initial dose should be given. This may be repeated at intervals throughout the operation. One has learned to identify certain types of individual who are particularly sensitive to the drug, and who will ride comfortably with satisfactory hypotension for an hour or more on an initial dose of 10 mg.

Suitable Cases

Type of Operation.—As hypotension is to a large extent postural and depends on the pooling of the blood in the dilated vessels, especially those of the legs, operations in which a foot-down tilt can be maintained are most suitable for the employment of this technique. For maximum success the surgical site should be elevated above the pelvis and legs. Thus operations on the head and neck, thorax, etc., have produced the most satisfactory results. Examples of such are a thyroidectomy, a large scalp rotation flap, and a mastectomy—all potentially "bloody" performances. In each of the three cases bleeding was minimal. The thyroid resembled a demonstration of anatomical dissection, the scalp-flap lower towel was almost dry at the end of the operation, and in the case of the mastectomy the towel below the axilla was devoid of its usual post-operative pool of blood.

Posture, however, is not everything, and considerable success has been achieved with patients in the lithotomy position for repair of the pelvic floor. (It is hoped to record this series in a separate communication.)

Type of Individual.—Patients with mild hypertension (say 180/100 mm. Hg) react very readily. As an initial dose 10 mg. of pentamethonium iodide may produce adequate hypotension (and a bloodless field) in a pelvic floor repair lasting 40 minutes. If the optimum

position is obtainable all types of individuals will respond, though tough, heavy, imperturbable males are inclined to be resistant and disappointing. I have so far had no experience of the technique with children.

Technique

Premedication may be according to taste. Personal preference is for "omnupon"—scopolamine. (Note the patient's pre-operative blood pressure, and any alteration under premedication. A marked fall denotes a probable sensitive reactor to methonium compounds.) Induction is with thiopentone or other barbiturate, followed by nitrous-oxide-oxygen, with or without cyclopropane to settle. Intubation can be carried out with or without a relaxant. As soon as composed, the patient should be tilted into a 20-degrees foot-down position. A Gordh needle, or a needle with a leak-proof cock, should be placed in a suitable vein, and the initial dose of pentamethonium iodide (or hexamethonium bromide) given. A sequence of blood-pressure readings are now taken. When the systolic reading is in the neighbourhood of 70 mm. or below (and not higher than 80 mm.), the surgeon may begin work. The fall to the necessary level usually takes place in three to five minutes. If subsequent movement of the patient is necessary to get an ideal operating position the blood pressure must be watched. If there is a rise further dosage of the methonium may be given, unless it can be lowered by slightly increasing the foot-down tilt. Maintenance of anaesthesia is usually with nitrous oxide and oxygen supplemented with a barbiturate, pethidine, or cyclopropane. The giving of small quantities of barbiturate in weak solution during profound hypotension does not seem to have any further effect on the blood pressure. I have usually avoided cyclopropane, owing to its occasional tendency to produce mild hyperpnoea.

The usual aim is to keep the systolic pressure between 60 and 70 mm. For the first half-hour or longer this is generally easy. If it falls below 50 mm., reducing the foot-down tilt will tend to raise it. The diastolic reading is often difficult to record accurately. In operations lasting from one-half to three-quarters of an hour the initial dose of the drug will usually prove sufficient. In longer operations additions of from 10 to 25 mg. of the drug may have to be given. Often increasing the table-tilt will prolong the action of a dose. There seems little benefit in lowering the systolic pressure below 60 mm. So far the longest period of maintained hypotension of 60 mm. has been 2½ hours. This was an extensive scalp-plastic operation in a woman of 38. She suffered no ill effects, her cerebral and renal functions subsequently being normal.

The blood pressure, either by posture alone or with the addition of further methonium, must be kept low until the skin is closed. Thereafter the patient should be raised to the horizontal and the blood pressure watched. If there is not a rise to above 80 mm. systolic, a slight head-down tilt may be adopted for two to three minutes. This will generally produce a rise to about 100 mm. systolic. If, however, the systolic pressure still remains below 80 mm., 10 mg. of "methedrine" will always raise it in from one to three minutes.

One word of warning here is necessary. If the lithotomy position has been adopted (as for a pelvic floor repair) and the blood pressure has been held satisfactorily low, care must be taken when the legs are

lowered. Flow of blood into the legs may produce a further drop of pressure, and a head-down position must be adopted at once.

Post-operative Phase

Great care must be taken in the immediate post-operative stage. The patient must be lifted flat on to the stretcher, and kept so on the way back to the ward. He must be wheeled head downhill on ramps or inclines, and lifted into bed with care to avoid raising the head and shoulders. The foot of the bed must be kept up on blocks until the anaesthetist has again seen the patient. The blood pressure is usually steady at 100–110 mm. in about two hours. No particular precautions are necessary after the blood pressure is stabilized. It usually returns to normal in 24 to 36 hours. Dilated pupils sometimes last for two days, rarely leading to a complaint of difficulty in reading during the first day. One of our cases had a very low temperature—95.6° F. (35.3° C.)—for six hours after operation. Vomiting was very slight, as one might expect after gas-barbiturate anaesthesia. My impression is that it was even less than usual. A few patients have complained of tiredness and lassitude for the first day. No major ill effects have been noted. There has been no case of prolonged hypotension, and no case of cerebral damage or alteration in function.

Dangers

The obvious dangers might seem to be: (1) Reducing the cerebral circulation below a safe level. In hyperpietics the sudden fall in blood pressure and diminution of circulation might be specially dangerous. (2) Ill effects of reduced circulation on other organs—for example, kidneys. (3) Prolonged effects of hypotension. (4) Post-operative secondary haemorrhage as the blood pressure rises again. (5) Danger during the unstable immediate post-operative stage; especially during transport and lifting into bed, etc. (6) Failure to establish hypotension initially or to maintain it throughout the operation, leaving the patient deprived of normal vascular tone and liable to increase bleeding.

Cautious approach to the subject suggests that these dangers are mostly theoretical. With full oxygenation of the blood, with vasodilatation as a result of the sympathetic block, and with a constant blood volume, sufficient circulation is maintained to prevent any organ falling into jeopardy. Even two and half hours with the systolic pressure below 60 mm. produced no subsequent alteration in function. Post-operative secondary haemorrhage has been conspicuously absent; in fact, we have seen it only once, and that in a forehead-flap rhinoplasty—a procedure which under other conditions has been known to lead to bleeding after operation. If methylamphetamine hydrochloride ("methedrine") has been given I suggest that the danger of subsequent haemorrhage is greater after the sudden rise in pressure which results. When a normal blood pressure is regained gradually the danger seems remote.

Danger during the movement after operation is very real. It is worth while here to repeat the warning already given. To ensure safety, some responsible and instructed person from theatre or ward must accompany the patient, and the blood pressure must be recorded immediately on his regaining the bed, and thereafter half-hourly. Methylamphetamine hydrochloride should be at hand, and be given in 10-mg. doses

if hypotension is prolonged. (In practice this has very rarely been necessary.)

Failure to achieve sufficient hypotension, or to maintain it, after autonomic ganglion block may lead to trouble. If bleeding appears to be severe, replacement therapy is the only measure likely to remove the danger to the patient. Fortunately, failure in suitably chosen cases is infrequent, and the results of failure are rarely serious. I personally have been worried by severe bleeding once only.

Summary

The production of hypotension during surgical operation by blocking the autonomic ganglion with a suitable methonium drug can produce operating conditions of great attraction to the surgeon, can considerably reduce bleeding and therefore add to the patient's safety and post-operative health, and seems to be a safe procedure in skilled hands and with constant observation. It must be realized that posture plays a large part in producing the desired level of hypotension, and therefore the technique is unsuitable for certain operations. Some individuals also appear unsuitable, and the individual reaction to the drugs used so far is variable.

It must be mentioned that success, or otherwise, in reducing haemorrhage in each individual case has been assessed entirely by the surgeon. Well over three-quarters of the 250 cases have been categorized as "good."

ADDENDUM

Since this paper was completed the subject has been debated at a meeting of the Anaesthetic Section of the Royal Society of Medicine, with papers from Drs. Enderby and Armstrong Davison. Although the work already done in this field is consequently more widely known, I feel that attention to the basic principles of the technique and the importance of careful selection of suitable cases cannot be overemphasized.

Recently a case has been brought to my notice where a patient died two days after an operation for removal of a malignant tumour involving skull and meninges. Hexamethonium bromide had been used to control severe haemorrhage. The patient's blood pressure apparently never rose above 80 mm. systolic during the two post-operative days, nor was any adequate attempt made to raise it. Anuria was absolute for the first 24 hours, but the kidneys excreted some urine during the second 24 hours. Two errors of technique seemed to me to have been made in this case. First, the drug was used late to control already established haemorrhage, instead of at the beginning to prevent bleeding. It is possible that the circulating blood volume had already been dangerously reduced by the time it was used. Secondly, hypotension was allowed to persist for too long without attempts to correct it by posture and methylamphetamine hydrochloride. I think it is absolutely essential, in using this technique, to maintain a full circulating blood volume and full oxygenation, and to use an adequate dose of the drug to produce successful block and consequent vasodilatation. If extreme hypotension is prolonged beyond a few hours, measures must be taken to correct it.

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TUBERCULOUS LYMPHADENITIS IN THE NIGERIAN AFRICAN

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Old-established conceptions of the pathogenesis of tuberculous lymphadenitis still appear to hold the field. Thus Boyd (1947) states that the cervical lymph nodes may become infected through one of two routes: either by the blood stream, in which case scattered nodes are attacked, or by the lymph stream. In the latter, which is much the commoner mode of infection and accounts for 90% of cases, the cervical nodes become involved via the lymphatics from a primary tuberculous focus in the tonsils, adenoids, or teeth caused by ingestion of contaminated material, notably milk from tuberculous cows.

Mitchell (1917), in Edinburgh, found 88% of cases of tuberculous adenitis in children to be due to the bovine bacillus, and demonstrated tubercle bacilli in 20% of samples of the local milk supply. In New York, Park (1910) found 34% of all cases, and 54% in children under 5, to be of bovine origin. In corroboration of the path of infection microscopical evidence of tuberculosis in the tonsils has been reported in 38% of cases, while tubercle bacilli have been demonstrated in the decayed dental root pulp of those harbouring tuberculous nodes. It should, however, be pointed out that the discovery of a tuberculous focus in a tonsil is by no means proof positive that this was the original portal of entry. A lymphatic organ such as the tonsil, endowed with generous lymphatic communications, might conceivably undergo retrograde infection from previously tuberculous cervical nodes.

There seems, however, to be considerable support for this conception in the case of bovine infection, though it does not appear to be applicable to all cases of tuberculous lymphadenitis. In civilized countries an increasing attention to the care of herds and to pasteurization has of recent years considerably reduced the proportion of cases attributable to bovine infection. In Southern Nigeria bovine infection is a rarity, but for a different reason. Relatively few cattle are driven down from the north, because tsetse belts have to be traversed *en route*, while fresh milk and butter do not enter into the dietary of Southern Nigerians. Peripheral tuberculous lymphadenitis among the latter may thus be taken as almost invariably due to infection with the human bacillus.

Some observations on the features of the disease in 51 consecutive cases seen in Lagos are here presented and the implications discussed. In 24 cases the diagnosis was made on clinical grounds alone, always quite typical, and in the majority with associated sinuses, cold abscess, pulmonary tuberculosis, or pleural effusion. In five cases the diagnosis was supported bacteriologically by gland puncture, in 10 cases histologically by gland biopsy, and in 12 by the macroscopic appearance at surgical excision with additional histological confirmation in five. Tuberculin tests were not carried out in this series.

Clinical Data of Present Series

Of the 51 cases 32 were male and 19 female; by European standards a relatively large number were