ABNORMAL RESPONSE TO SUXAMETHONIUM IN POLYARTERITIS NODOSA

BY

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Polyarteritis nodosa is a disease in which widespread acute necrosis occurs in the arteries, leading to a variety of functional disturbances involving the nervous system, heart, kidneys, lungs, abdominal viscera, and blood (Harvey, 1959). The liver is affected in this condition more frequently than is recognized. The following case report illustrates the need for care in the administration of muscle relaxants to patients suffering from polyarteritis nodosa.

CASE REPORT

A male, J. W., aged 60, occupation a railway checker, was admitted to hospital on August 6, 1960, complaining of swelling and pain in the hands, with blueness of the tips of the fingers for two weeks. There was nothing of relevance with respect to personal history, family history or previous diseases. Three to four months before admission he began to get aching pains in both hips and was told that it was lumbago. This pain recurred on and off for about two months. Five weeks prior to admission pain began in his calves which did not get better with rest and he was referred for physiotherapy. However, he did not improve with treatment and three weeks later his fingers began to swell and the nail beds went blue: this was followed a few days later by swelling of the backs of the hands and the cyanosis spread to involve the distal phalanges.

Examination on admission revealed auricular fibrillation. Peripheral pulses were present and the blood pressure was 210/100 mm Hg. He was moderately emphysematous. Examination of the hands revealed swollen index, middle, and little fingers of both hands. The terminal phalanges were blue. Examination of the heart and abdomen revealed no abnormality. A provisional diagnosis of polyarteritis nodosa was made.

He was treated with tolazoline and achromycin initially and 11 days later he was given prednisolone. Nevertheless 16 days after admission the blueness had extended, accompanied by blistering; at this stage heparin therapy was started. The next day he had developed a nodular lesion on his right buttock and an area of blueness on the dorsum of his right foot. As a result of the latter it was decided that a retrograde aortogram should be carried out.

Investigation up to this time had revealed a raised E.S.R. (75 mm 1st hour), fasting blood sugar of 89 mg/100 ml; plasma uric acid 4.3 mg/100 ml; urine no abnormal constituents; serum cholesterol 220 mg/100 ml; cold agglutinins nil; Hb 80 per cent; total proteins 6.4 gm/100 ml. Electrophoresis showed a reduced albumin and a slightly raised alpha-2 globulin with no abnormal fractions. There was no eosinophilia.

Retrograde aortogram and biopsy of skin. Premedication consisted of pethidine 50 mg and atropine 0.6 m.g. i.m. 1 hour before induction of anaesthesia. The latter was carried out with a cyclopropane and oxygen mixture in a closed circuit. When adequate relaxation had been achieved following the administration of 25 mg of suxamethonium chloride an armoured No. 10 latex tube was passed, after topical anaesthesia of the cords had been induced with 4 per cent lignocaine. Ventilation was maintained with 75 per cent nitrous oxide and 25 per cent oxygen. Spontaneous respiration did not return until 40 minutes after the administration of suxamethonium. Subsequently anaesthesia was maintained with nitrous oxide, oxygen and halothane. This was discontinued 1 hour after induction, on completion of the investigation.

Recovery was normal and there was no postoperative respiratory insufficiency. Some hours after the aortogram, it was noticed that pulses were absent in the right leg and a diagnosis of femoral artery thrombosis was therefore made; it was decided that thrombendarterectomy was necessary.

For his second anaesthetic premedication consisted of pethidine 50 mg and atropine 0.6 m.g and anaesthesia was induced with thiopentone 150 mg and suxamethonium 25 mg. (Owing to an unfortunate series of circumstances no record of the previous abnormal reaction to the relaxant drug was available to the anaesthetist on this second occasion). After intubation with a No. 10 cuffed endotracheal tube, the lungs were rhythmically inflated with a nitrous oxide and oxygen mixture and, as before, spontaneous ventilation did not return until 40 minutes after the administration of the suxamethonium; at this time the skin was being sutured. The patient was returned to the ward and postoperative recovery was uneventful.

The second anaesthetist subsequently ascertained that prolonged apnoea had occurred after the previous administration of suxamethonium and it was therefore decided to estimate the serum cholinesterase content. This was done 2 days later and found to be 7µCO₂/min. As a result the liver function was tested and the results were as follows:

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Direct Van den Bergh  Negative
Serum bilirubin  0.4 mg/100 ml
Zinc turbidity  3 units
Thymol turbidity  2 units
Thymol flocculation  Negative
Colloidal gold  Negative
Albumin  2 g/100 ml
Globulin  4.2 g/100 ml
Total protein  6.2 g/100 ml
A/G ratio  0.5/1
Alkaline phosphatase  32.3 K.A. units/100 ml

*The normal range for serum cholinesterase is 53–102 μlCO₄/ml/min with a mean value of 76 μl (Thompson and Trounce, 1956).

Histological examination of the skin biopsy confirmed the provisional diagnosis of polyarteritis nodosa.

Subsequent repeat liver function tests showed a gradual return to normal and four months later the cholinesterase level was found to be 44 μl CO₄/ml/min with an E.S.R. of 21 mm 1st hour. There had been no further progress of the disease process as evidenced by the lesions of the extremities.

**DISCUSSION**

An association has previously been noticed between certain of the so-called “collagenoses” and the myasthenic state: the diseases referred to are polymyositis, dermatomyositis, and systemic lupus erythematosus; the muscle weakness has responded to neostigmine (Rees and Harman, 1950; Bondonelle, Bouygues and Coulon, 1955).

Commenting on the anaesthetic technique in such myasthenic states, McClelland (1960) has pointed out that the use of muscle relaxants is contraindicated by an abnormal response of the neuromuscular junction.

Further, it has been noted that significant liver dysfunction can occur in polyarteritis nodosa (Rose and Spencer, 1957) and to this must be added lupus erythematosus ( Jessar, Lamont-Havers and Ragan, 1953). In these illnesses there is often surprisingly little clinical evidence to suggest liver dysfunction. However, Jessar and his colleagues found that of 15 autopsy examinations in lupus erythematosus, 4 had hepatic lesions; whilst Harvey and his co-workers (1954) found 40 cases of hepatic involvement out of a total of 84 autopsies in cases of polyarteritis nodosa.

A low cholinesterase level is a recognized feature of impaired liver function (McArdle, 1940).

The presence of either of the latter two of this loosely associated group of diseases thus furnishes a further possible contraindication to the use of a muscle relaxant, in this case suxamethonium; should general anaesthesia become necessary.

It will also be recalled that Dundee and Gray (1953) focused attention upon the observation that patients with liver dysfunction were more resistant to d-tubocurarine than normal healthy subjects. They suggested, in explanation, an association with the pseudocholinesterase level, which if low might reasonably be reflected in a higher than normal concentration of acetylcholine at the motor endplate requiring more d-tubocurarine than usual to produce paralysis.

There thus appears to be an indication to use d-tubocurarine rather than suxamethonium in the presence of polyarteritis nodosa or lupus erythematosus. However, in one of the above-mentioned diseases, lupus erythematosus, there are reports of both a myasthenic state and significant liver dysfunction.

There is no evidence to suggest that these abnormalities were co-existent: nevertheless it seems safest to avoid, or use with great caution, any muscle relaxant, depolarizing or nondepolarizing, in such circumstances until one is in a position to rule out the possibility of a myasthenic state on the one hand, or liver dysfunction on the other.

This case report underlines three important factors. Firstly that impaired liver function may be an unrecognized feature of polyarteritis nodosa in the absence of clinical signs, and secondly that liver involvement is not an infrequent occurrence. Thirdly it stresses the importance of adequate, readily available, anaesthetic records and emphasizes the desirability of a pre-anaesthetic serum cholinesterase estimation in this disease (particularly during an exacerbation) if the use of suxamethonium is contemplated.

**SUMMARY**

Prolonged apnoea occurred following suxamethonium administration to a patient suffering from polyarteritis nodosa.

The relationship between some of the “collagenoses” and significant liver dysfunction is discussed.

It is concluded that all muscle relaxants should be avoided or used with extreme caution, in the presence of polymyositis, dermatomyositis, systemic lupus erythematosus and polyarteritis nodosa, unless prior investigations of hepatic function have been found to be normal.
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REFERENCES


BOOK REVIEW


This book, which, as the Preface says, is a reprint with minor modifications, of Chapter V, Vol. I, of General Anaesthesia, edited by Frankis T. Evans and Cecil Gray, is designed for anaesthetists and surgeons who require information on the basic aspects of general neurophysiology. There have been so many recent advances in neurophysiology of particular importance to anaesthetists that a book of this sort should be especially welcome. Perhaps the most important to anaesthetists of all recent experiments are those relating to the mechanisms for consciousness and unconsciousness. The fundamental experiment that changed all previously held ideas about consciousness was that performed by Moruzzi and Magoun in 1949. They showed that repetitive stimulation of the reticular formation in the brain stem induced e.g. arousal. The extent of the control exercised by the reticular system on other brain mechanisms has yet to be defined but appears to be very wide indeed. Other recent experiments have shown that the reticular system itself is under the control of other brain mechanisms, particularly cortical. In fact we are beginning to realize that it is the brain as a whole that must be studied rather than its individual components. It is very disappointing, therefore, to find that all this work remains almost unmentioned in this book. The first half deals very adequately with the physiology and pharmacology of neurons and the physiology of synaptic transmission. The latter half of the book deals with cerebral circulation and metabolism and the physiology of the cerebro-spinal fluid. All this is well done and covers important subjects, particularly the effects of hypothermia. There are, however, only some twenty pages in the middle of the book, entitled "Electrical activity of the brain", which cover electroencephalography and touch lightly on the neurological basis of general anaesthesia. The section on electroencephalography is very much simplified, perhaps over much, since no mention is made of the great individual differences that exist from person to person. For example, it is suggested that everybody has an alpha rhythm which is responsive to opening and shutting the eyes. In fact, only about two-thirds of the population have this type of rhythm. The possible function of the alpha rhythm is not discussed at all, and the great dissociation that often exists between consciousness and unconsciousness is ignored. Perhaps the most striking example of this is the action of atropine on the dog. Under the influence of this drug the animal is obviously alert and wide awake, yet the electroencephalogram is like that of a sleepy animal. The effects of hyperventilation also are very variable. There is a section on the electroencephalographic monitoring of anaesthesia in which it is suggested that the electroencephalogram will always give a precise and accurate indication of the depth of anaesthesia in any particular subject. Recent experiments have suggested that this is by no means always so. In a mere two pages, entitled "A neurological basis for general anaesthesia", is considered, or rather, left unconsidered, the workings of the reticular system and the whole problem of the mechanisms for consciousness and unconsciousness. In the introduction to this book Dr. Wyke says that no reference is made to the special physiology of the sensory, motor or visceral nervous system. In the only mention of pain in the book, and surely pain is important to anaesthetists and surgeons alike, Dr. Wyke says that "it is important for the anaesthetist to realize that even in a deeply anaesthetized patient volleys of impulses from peripheral sensory receptors, especially pain receptors, continue to bombard the sensory sectors of the cerebral cortex through the thalamo-cortical relays thereto". Recent work makes it almost certain that there is nolemniscal pathway for pain, and that painful stimuli travel up the cortex only via the secondary extralemniscal pathways. These secondary pathways are particularly susceptible to anaesthetic agents, and it is practically certain that no painful stimuli reach the cortex during very light anaesthesia.

On the whole this book appears to follow the classical approach to neurophysiology in that it considers the workings of individual units rather than the workings of the brain as a whole, and it is becoming clear that it is the working of the brain as a whole that is of particular importance to anaesthetists.

There is a table of contents designed to guide the reader to any particular section of the book, but surely if a book of this sort is worth reading it is worthy of an index?

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