This greatly lessens the amount of sedative needed by preventing pain. Here again the use of the machine was a big advantage and we tried to run it at about 60°F., which would keep the temperature in the stump slightly lower than room temperature. The claim of freedom from shock during operation was well substantiated. . . . There were five deaths in hospital, the earliest, the second day postoperatively and the latest after one month. . . . The thirteenth case deserves special mention. This was a mid-thigh amputation in a diabetic woman of 65 who was in good condition. It was an attempt to try out refrigeration by packing the leg in ice without the use of the tourniquet. At the Ottawa General Hospital where this was done, the experience with refrigeration anaesthesia had not been favourable. Of six cases one had died the third day, in two the healing was satisfactory, in two it was poor and in the sixth it was so bad that the patient finally died of sepsis following a secondary amputation under cyclopropane. . . . In spite of morphia and nembutal, the patient complained bitterly of the coldness of the pack. After an hour and a half when the distress did not appear to be lessening, we were about to take the whole thing off, when it was suggested we try small doses of intravenous pentothal. General body chilling occurred, the patient became blue and shivering and mouth temperature went down to 96°F. The pack was on five and a half hours yet there was not complete anaesthesia for the operation. . . .

"This whole subject of refrigeration may still be said to be controversial because of the healing factor. Yet I am convinced it should hold a real place in surgery both as a therapeutic agent and as an anaesthetic."

J. C. M. C.

VINING, J. A.: *Supportive Treatment During Anaesthesia.* Canadian M. A. J. **57**: 479–484 (Nov.) 1947.

"The surgeon has become more and more dependent upon the judgement of his anaesthetist for pre- and postoperative advice, in the treatment of his patient. The surgeon, however, still relies upon his anaesthetist chiefly for his skill in the administration of the anaesthetic and for his supportive treatment during the anaesthetic period. . . . Respiratory movements should at all times be under the direct observation of the anaesthetist. . . . The mechanical control of normal respiration depends upon a free airway and intact thorax. The vital capacity and tidal air are limiting factors. . . . The observations of skin colour and temperature provide information regarding the physiology of circulation and respiration. . . . The chief concern of the anaesthetist with regard to heat regulation during anaesthesia is its loss. . . . The mental state of the patient is important to the anaesthetist in its effects upon the other systems of the body. . . . In his supportive treatment during the anaesthetic period, the anaesthetist must direct his treatment to approach as closely as possible the normal physiological standards. His methods of control must follow his knowledge of physiology and pharmacology. In other words, he must follow his observations and must not be led astray by empirical thinking."

J. C. M. C.

STEPHEN, C. R., AND CHANDY, J.: *Clinical and Experimental Studies with Myanesin; A Preliminary Report.* Canadian M. A. J. **57**: 463–468 (Nov.) 1947.

"In December, 1946, following an investigation of numerous a-substituted ethers of glycerol, Berger and Bradley reported on the pharmacological prop-

erties of a:b dihydroxy-y(2 methylphenoxy) propane. This compound, which they named myanesin, produced transient relaxation and paralysis of skeletal muscles in animals, and showed a wide margin of safety between paralyzing and lethal doses. . . . Shortly after, in a series of 112 clinical cases, Mallinson discussed its value and safety as a muscle-relaxing agent when used as an adjunct to anesthesia. These observations prompted the present study to gather information on the site or sites of action of this drug, in order to evaluate more fully its therapeutic usefulness. For this purpose clinical trials, aided by electroencephalograms, have been carried out on a number of patients, and certain experimental data have been recorded. . . . Myanesin was administered alone to patients in an arbitrary dosage of 30 mgm. per kg. of body weight. The drug was given into an arm vein in 10% solution at a rate of 1 to 2 c.c. per minute. Clinical reactions were noted closely and on seven patients electroencephalograms were recorded before, during and after injection, using the standard scalp surface and ear electrodes, as well as the basal electrode placed in the posterior nasopharynx for recording the electrical activity of deep-lying cerebral structures. . . . The cases to be reported can be classified into three groups: (1) patients suffering from diseases of the extrapyramidal nervous system; (2) those having frequent recurrent intractable pain; (3) patients with known spinal cord lesions. . . . Up to the present myanesin has been administered on some 50 different occasions. . . . With one important exception, no significant alterations in pulse or blood pressure were evident during or after the injection. . . . Almost all patients complained of a hot or flushed feeling during administration and usually the face and neck became reddened temporarily. One patient who was receiving the drug in the sitting position developed a sudden syncope after administration of 2.0 c.c. This was explained as an acute cerebral anaemia coincident with the noted signs of widespread vasodilatation while in the sitting posture. . . . There were no subjective complaints of difficulty in breathing and no evidence was noted of intercostal paresis. In two patients there was slowing of the respiratory rate, but it did not fall below twelve per minute. . . . With the dosage given, none of the patients went to sleep, nor were any sleep patterns seen in the electroencephalograms. . . .

"During administration no apprehension was felt, but most patients complained of feeling 'dopey,' 'relaxed' or 'heavy.' After completion of the injection the dopiness disappeared within 2 to 3 minutes, but the relaxed feeling persisted for about an hour. Most patients exhibited a mild degree of euphoria during this latter period. . . . Apart from relief of presenting symptoms . . . the principal neurological alteration seen in all patients was a coarse nystagmus present in all directions, associated with inability of the eyes to converge. . . . Voluntary motor power, determined clinically and by objective measurement, was not decreased in any patient. Also, pain reaction to pinprick showed no alteration. Superficial and deep reflexes were unchanged. . . . Within eight hours of administration, ten patients noted that their urine was reddish-brown in colour. One case reported dysuria and frequency for several hours. Examination of the altered urine showed no leucocytes or erythrocytes, but the orthotolidine test for blood was strongly positive, and small quantities of albumen (30 to 100 mgm. %) were present. These findings indicated that in some patients the administration of myanesin produced haemolysis of blood. No traces of blood were seen in specimens

passed more than eight hours after injection. . . . Seven patients experienced about the site of injection some degree of inflammatory reaction which appeared clinically to be a localized thrombophlebitis. The soreness and redness disappeared completely within 48 hours of its appearance. . . . The electroencephalographic studies carried out with seven of the patients showed no evidence of significant alteration in the electrical activity of the cortex with the maximum doses of myanesin employed. In certain cases which displayed increased nervous tension, the increase in normal alpha rhythm following myanesin suggested a degree of general relaxation. However, no slow waves, which might indicate a depression of cortical function, were observed. Abnormal waves recorded from the base of the brain—probably diencephalic in origin—disappeared from the electroencephalogram with the disappearance of the clinical signs and symptoms. . . .

"Twenty-five experimental studies on eight cats were carried out with the object of studying the action of myanesin on nerve conduction, the neuromuscular junction and synaptic transmission within the cord. These experiments were performed three to twenty-four hours after transection of the spinal cord at the lower thoracic levels. The nerve and muscle action potentials were recorded on the cathode ray oscilloscope. . . . From the animal experiments it may be concluded that, until relatively large doses are given, myanesin has no effect on transmission of nerve impulses through the synapses of the spinal cord, on conduction of impulses along a nerve, or on transmission of impulses across the myoneural junction. These facts tend to be corroborated by the absence of clinical observations that the drug has any peripheral nerve action in a dosage of 30 mgm. per kilo. In considering action on the cerebral cortex and brainstem, most of the evidence accumulated is clinical in nature. The nystagmus seen in every case suggests a possible action within these structures. However, in the doses specified, voluntary motor power and sensation are not interrupted, thus indicating that the corticospinal tract, and indeed the final common pathway to the periphery, are not affected. Also it is notable that the waves from the cortical leads of the electroencephalogram show little change with the drug administration. Thus there is little evidence of direct action on the cerebral cortex. . . . It is impossible to state as yet any opinion regarding the therapeutic value of this compound. When given intravenously, it has a shortlived beneficial effect on certain diseases of the extrapyramidal nervous system and on pain of central origin. The localized thrombophlebitis at the site of injection and the transient evidence of haemolyzed blood in the urine seen in some patients are untoward reactions which will bear careful evaluation against the beneficial effects of the drug. It is hoped that this preliminary report will prove an impetus for further investigation of drugs of this nature."

J. C. M. C.