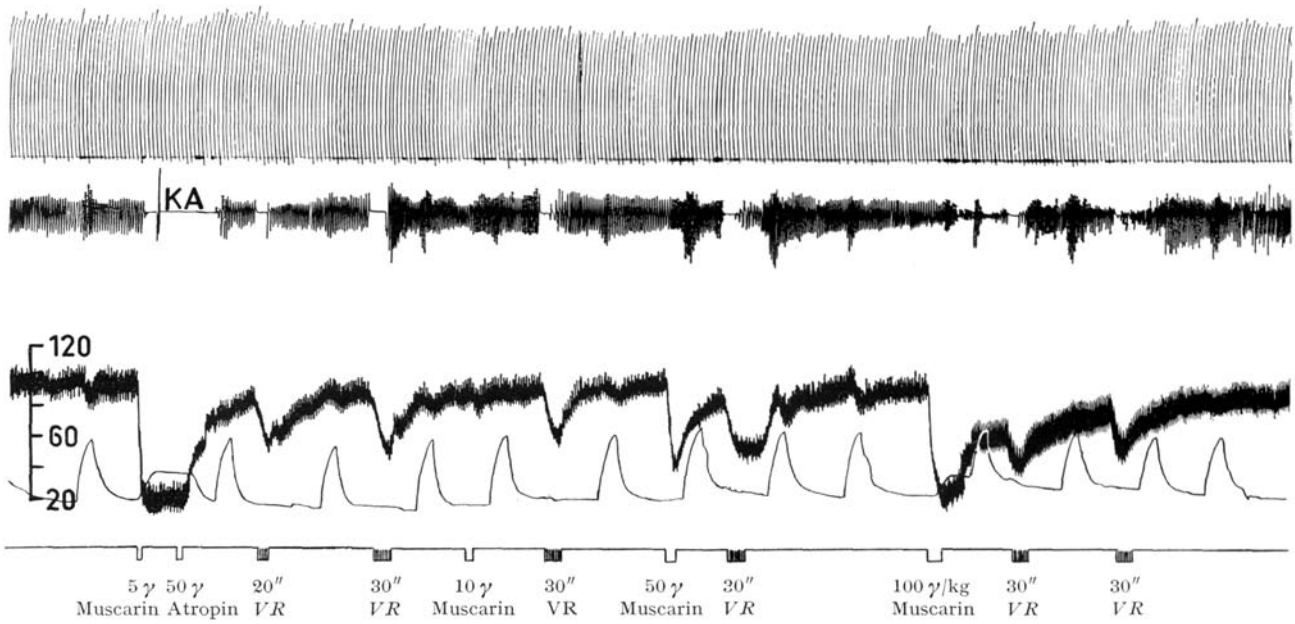

Abb. 2. Katze in Dial-Nembutal-Narkose. *VR* = Vagusreiz während 20 oder 30 s. Dosen ebenfalls in γ = μg/kg Katzengewicht. Muskelzuckungen alle 7,5 s.

demonstriert ist (Abb. 1 und 2). Atropin hat erst bei hohen Dosen eine ganglionhemmende Wirkung; KONZETT und ROTHLIN[1] blockierten das isolierte *Ganglion cervicale superius* mit 0,5–5 μg. Auch der Parasympathicus ist nicht beeinträchtigt: eine vagal durch präganglionäre Reizung ausgelöste Blutdrucksenkung wird zu der durch Muscarin bewirkten Depression addiert (Abb. 2). Innerhalb einiger Minuten wiederholte Injektionen der gleichen Dosis haben keine kumulativen Effekte zur Folge (Abb. 1).

c) *Sehr grosse Dosen* ($>$ 10 μg/kg) können nur beim atropinisierten Tier untersucht werden, um die letale, peripher parasympathomimetische Wirkung zu unterdrücken. Meistens mussten wir auch künstlich beatmen. Atropin antagonisiert eine proportionale Muscarindosis (etwa $^1/_{100}$) in der Blutdruckwirkung. Grössere Muscarinmengen oder Vagusreizung senken den Druck immer noch bedeutend. Die Synapsen der sympathischen Ganglien sind in ihrer Überleitung unverändert. Bei Vagusreizung nach wiederholten grossen Dosen (10–100 μg/kg) zeigt sich eine immer gleichbleibende Blutdrucksenkung, Herzschlagverlangsamung und Atmungsstillstand (Abb. 2).

Zusammenfassend stellen wir fest, dass Muscarin in Dosen, wie sie vom Ganztier noch ertragen werden, eine rein periphere parasympathomimetische Wirkung hat. Auch nach sehr grossen Dosen (bis 20000fache minimale Wirkungsdosis) werden beim atropinisierten Tier weder vagale noch sympathische Ganglien blockiert, und die Muskelendplatten bleiben voll funktionstüchtig. Muscarin hat demnach keine «nikotinische» Wirkung, sondern ist (bis 100 μg/kg) elektiv an den parasympathischen Endigungen wirksam. Die früher wiederholt beschriebene «Vaguslähmung» muss eine Folge der Verunreinigung mit Cholin und anderen (quartären?) Basen sein.

Cholinesterasehemmung verstärkt die Muscarinwirkung um das 10fache, vielleicht weil ein Ester des Muscarins (Azetylmuscarin?) im Körper wirksam ist. Ein rascher enzymatischer Abbau ist auch durch die kurzdauernde Wirkung und das Fehlen von Kumulation wahrscheinlich.

[1] H. KONZETT und E. ROTHLIN, Helv. physiol. Acta *7*, C 46 (1949).

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Summary

High doses of Muscarine have only peripheral parasympathomimetic action in the cat. Even with toxic doses (up to 100 μg/kg) the atropinized animal shows no blockade of sympathetic and parasympathetic ganglia or nerve-muscle transmission. Inhibition of Cholinesterase enhances Muscarine activity tenfold, suggesting that Muscarine is transformed in the body into an active Acetylester.

The Effect of Xylocain in Electric Convulsive Treatment

In recent investigations on "experimental epilepsy', it was shown by BERNHARD and BOHM[1] that intravenous injections of local anaesthetic shorten or abolish the cortical after-discharge evoked by repetitive electrical stimulation of the cortex depending on the dose. On the basis of animal experiments, the effect of xylocain was later investigated in epileptics, and it was shown that epileptic fits of grand mal type or Jackson type could be arrested by intravenously injected xylocain[2]. The electroencephalographically recorded convulsive activity evoked by photic stimulation in epileptics may also be blocked by xylocain[3]. No untoward reactions

[1] C. G. BERNHARD and E. BOHM, Acta physiol. Scand. *31* [suppl. 114], 5 (1954); Exper. *9*, 474 (1954); Brit. J. Pharmacol. *10*, 288 (1955).

[2] C. G. BERNHARD and E. BOHM, Acta physiol. Scand. *31* [suppl. 114], 5 (1954); Exper. *9*, 474 (1954). – C. G. BERNHARD, E. BOHM, and S. HÖJEBERG, Arch. Neurol. Psychiat. Chicago, *74*, 208 (1955).

[3] C. G. BERNHARD, E. BOHM, S. HÖJEBERG, and K. A. MELIN, Acta psychiat. Kbh. (in press).

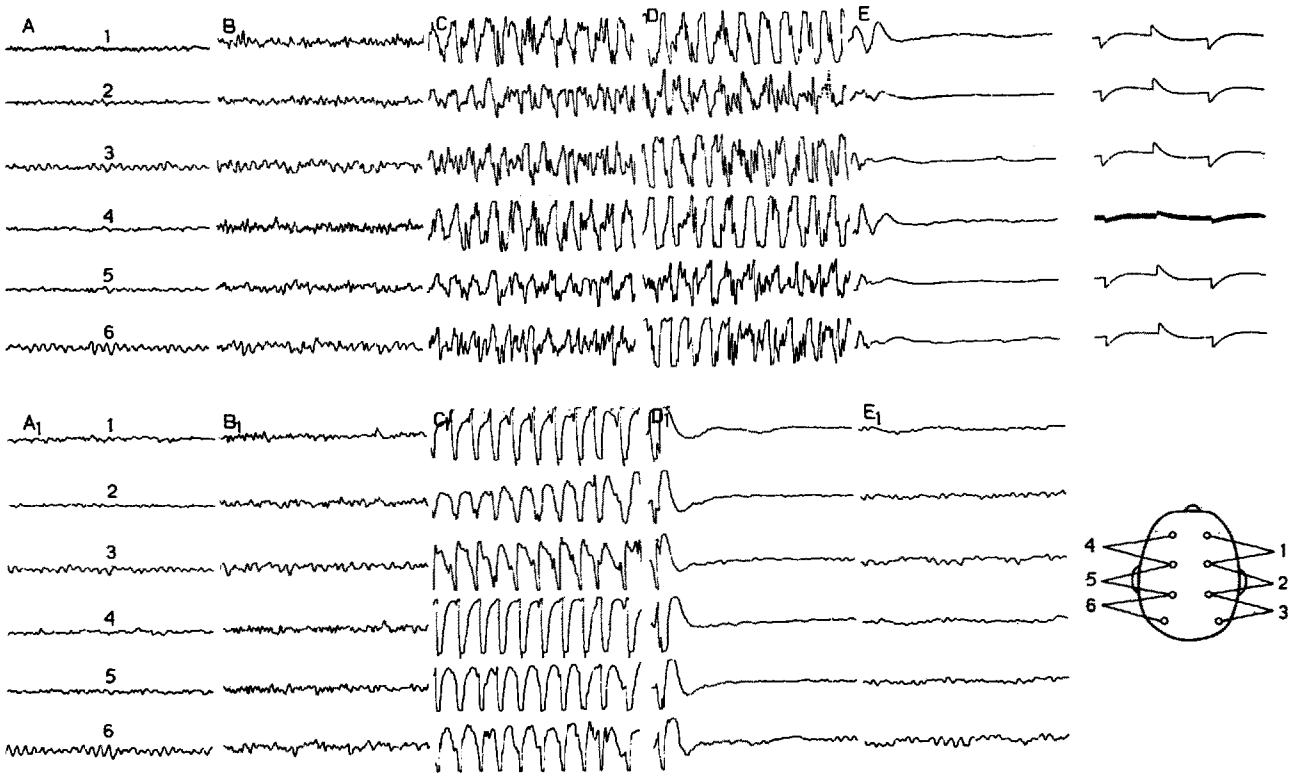

Fig. 1.–EEG. during the course of an electric convulsive treatment without (A–E) and with (A_1–E_1) an intravenous of 3 mg Xylocain per kg 2 min before the shock was elicited.. The after-discharge is reduced to 25% of its previous duration. For further description see text. Calibration 50 μV.

were noticed. Contrary to general belief, there was no sign of xylocain acting as a convulsive agent. The duration of the anticonvulsive effect in humans after single intravenous injections of xylocain was about ½ h with the doses used.

The investigations referred to provide a basis for an examination of the effect of xylocain in electric convulsive treatment. The present investigation comprises a series of 25 injections in 10 patients; and it has been found that xylocain shortens the duration of the cortical after-

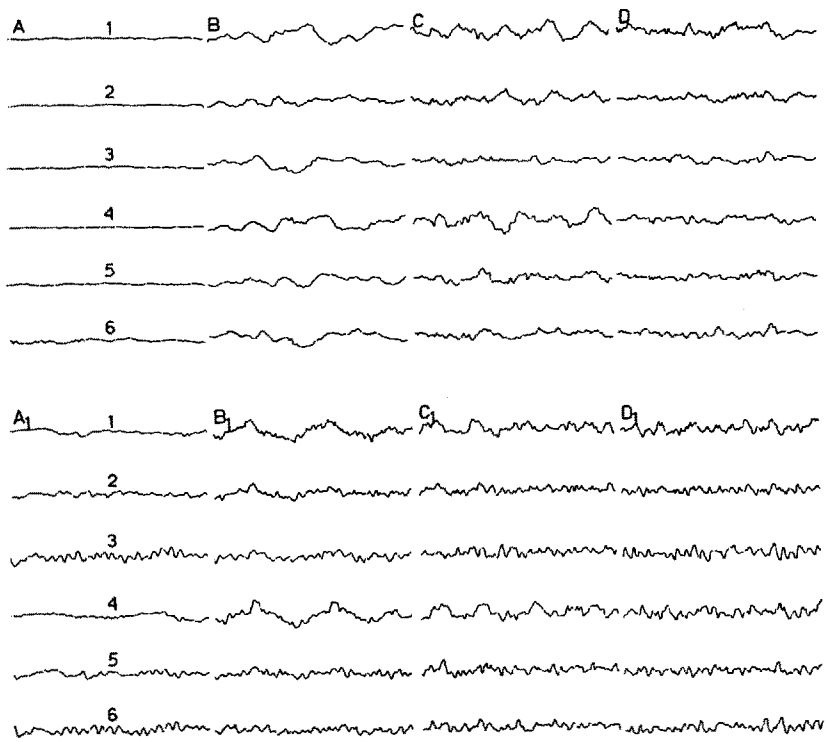

Fig. 2.–Post-epileptic EEG. at various intervals after the end of a spontaneously terminated after-discharge (upper row) and an after-discharge shortened by Xylocain (lower row). Further description see text.

discharge principally in the same way as in the animal experiments.

In all treatments the patients were given a light evipan anaesthesia (5 mg/kg), saturated with oxygen and paralyzed by an adequate dose of succinylcholine iodide. The shock was delivered by a "Konvulsator III" according to V. BRAUNMÜHL. The cerebral electrical activity was recorded by a six-channel Grass electroencephalograph. The position of the recording electrodes are shown in Figure 1. One or two treatments were first given without xylocain in order to estimate the duration of the post-stimulatory cortical after-discharge, which was found to be fairly constant from treatment to treatment in the same patient. The dose of intravenously injected xylocain ranged between 2–4 mg/kg and a supramaximal shock was delivered 2 min after the end of the injection. The dosis of xylocain ranged between 2–4 mg/kg injected intravenously during 1 min and a supramaximal shock was delivered 2 min after the end of the injection.

Figure 1 *A–E* show the electroencephalograms during the course of an unmodified treatment. Record *A* shows the EEG. prior to any injections. Evipan and succinylcholine were then administered and record *B* shows the EEG. immediately before the shock. The shock was then delivered through bitemporal electrodes and the following records (*C* and *D*) show the after-discharge 10 s (*C*), and 25 s (*D*), after the cessation of the repetitive stimulation. Record *E* shows the spontaneous cessation of the cortical after-discharge and the post-epileptic depression of the cortical activity 1 min 40 s after the end of the shock.

Records A_1–E_1 in Figure 1 are from the same patient and show the effect of an intravenous injection of 3 mg xylocain per kilogramme. The extracts from the EEG. are taken at the same intervals. Record C_1 shows the convulsive activity which is more regular and monotonous than in the corresponding curve above. Record D_1 shows that the after-discharge was blocked 25 s after the end of the stimulus. In record E_1 there is already a restitution of pre-treatment activity.

In the present series the duration of the after-discharge was reduced by 60–80% following pre-treatment administration of xylocain. There was no certain tendency to a greater effect when the dosage of xylocain was increased to 4 mg/kg.

The EEG. was regularly followed for 30 min after the shock. In Figure 2 the EEG. is shown immediately after (*A*; A_1) and 3 (*B*; B_1), 10 (*C*; C_1) and 20 min (*D*; D_1) after the end of the after-discharge without (upper row: *A–D*) and with (lower row: A_1–D_1) xylocain. Without xylocain, there was a greater degree of depression of the cortical activity following upon the longer after-discharge than after a xylocain injection, and probably a more pronounced dysrhythmia with slow waves.

There were no complications and no complaints from the patients which could be ascribed to the xylocain treatment. It should be pointed out, however, that the intravenous use of the drug must be handled with great care until more experience has been collected.

The experiments were made in order to elucidate the significance of the after-discharge for the clinical effects of electric convulsive treatment.

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Zusammenfassung

Es hat sich gezeigt, dass Xylocain in kleinen intravenösen Dosen die epileptiformen Nachentladungen bei Elektroschockbehandlung abkürzen kann. Die Untersuchungen werden fortgesetzt, um die Bedeutung der Nachentladungen für die klinischen Effekte der Elektroschockbehandlung zu beleuchten.

Insulin and its Possible Role in the Artificial Hibernation

Artificial hypothermia or hibernation has been studied during recent years as a means of reducing the oxygen consumption of the tissues and thus allowing surgical treatment of various cardiac and vascular diseases. It is known, however, that the decrease of body temperature in the homeothermic organism is constantly followed by metabolic and cellular changes of importance. The need was therefore emphasized of reducing such disadvantages by various techniques and drugs[1]. Substances with a ganglioplegic action have acquired a special importance in this field. Such drugs reduce the changes produced by the body hypothermia but do not prevent some of the reactions of the homeotherm to the hibernation.

In fact, in animals treated with such drugs, some rather important changes of certain physiological constants have been observed (glycaemia, lipaemia, heart rate, endocrine activity), as well as the presence of shivering and shock post-hibernation, which has not yet been given a clinical or experimental explanation[2]. As a matter of fact, a homeotherm organism reacts to any decrease of body temperature with an increased metabolic rate and an increase of the organic combustions with the object of keeping its own temperature constant. In this way not only its lipidic and glycidic reserves but also the proteic ones and its enzymatic patrimony are wasted.

Having regard to these facts, it seems to us that the ganglioplegics are not sufficient to prevent the dangerous increase of organic combustions, and that it is therefore necessary to act directly on the cellular metabolism by means of some substances possessing an antagonistic action on the hormones of which production is stimulated by hypothermia. Our attention was drawn to insulin.

In fact, insulin decreases the blood sugar, increases the hepatic and muscle glycogen (which disappears rapidly with the hypothermia), favours lipogenesis, diminishes the use of O_2 by the tissues, showing a clear anabolic and hypothermic action. Such a conception has also been supported by the fact that in the hibernant

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