The quaternary steroid was tested either as the iodide, M & B 9105, which is about 1% soluble in water at room temperature, or as the freely soluble chloride, M & B 9105A. Both salts form neutral solutions which can be sterilized by boiling. The compound was examined in several animal species.

In the rabbit, cat and monkey the quaternary steroid produced a flaccid paralysis of short duration, when injected intravenously, the onset of paralysis being noted by drooping of the head and loss of muscular tone in the limbs. As soon as the effect was observed, the injection was stopped so that respiration was not impaired to any extent. The doses in mg/kg of cation necessary to produce paralysis were 0.033 ± 0.002 (rabbit), 0.034 ± 0.013 (monkey) and 0.063 ± 0.006 (cat), whilst the duration of action ranged from 40 to 234 sec, being shortest in the rabbit.

In cats under chloralose anaesthesia, intravenous injection of M & B 9105 produces a short-lasting block of transmission from the sciatic nerve to the tibialis muscle. The block can easily be antagonized by an anti-cholinesterase such as neostigmine, or by a tetanus applied to the nerve. That the block was of a competitive nature, and not of the depolarizing type, was shown by the ability of the compound to antagonize the twitch caused by the close arterial injection of acetylcholine. Further evidence of the mode of action of M & B 9105 was provided in experiments in the conscious chick and in the hen under pentobarbitone anaesthesia. In both it caused a flaccid paralysis unlike the contracture found with suxamethonium. Although experiments in the rabbit, chicken and cat showed the duration of action to be similar to that of suxamethonium, in the monkey it had a longer effect, similar to that of gallamine. In man[6] the effect was similar to that found in the monkey. M & B 9105 has been found to be devoid of androgenic, oestrogenic and progestational activity.

Several views have been put forward relating neuromuscular paralysis to the size, shape and other properties of active molecules. Synthetic compounds with two quaternary heads have been for the most part flexible molecules, and peak activity has usually been observed when the nitrogen atoms are connected by ten other atoms, equivalent to a maximum separation of about 14 Å[7-9]. None of the four possible stereoisomers of *d*-tubocurarine is rigid, and an examination of models shows that the maximum interquaternary distance is 11–12 Å[9,10].

Flexibility of the molecule, however, is not essential for this type of activity. The cation of M & B 9105 is a rigid structure with the quaternary centres separated by nine carbon atoms, giving an inter-nitrogen distance of about 11 Å. For malouétine the ring system is similarly rigid, but the inter-nitrogen distance can vary from 11 to 12.5 Å, because of rotation of the side chain.

Fuller details of the pharmacology of M & B 9105 will be reported elsewhere.

Résumé. Un stéroïde quaternaire ($3\beta,17\beta$-dipyrrolidin-1'-yl-5α-androstane bisméthiodide) administré par voie intraveineuse provoque une paralysie neuromusculaire compétitive d'une durée fugace chez le lapin, le poussin, le chat et le chien, mais l'action est un peu plus prolongée chez le singe et chez l'homme.

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Indirect Effect of Ultrasound on Water Permeability of the Connective Tissue

Great importance is attached to the changes in permeability of biological membranes under the effect of ultrasound[1,2]. The ionization of water, production of peroxides and other chemically active compounds can play an important role in the mechanism of this biological effect[3]. In order to prove the possibility of such an indirect effect, the following experiments were performed.

To follow the process of permeability of a liquid irradiated by ultrasound, the principle of DAY's method[4] applied to the connective mesenteric membranes of rats was used[5]. The membranes were fixed to the end of a glass tube and the time of flow of 2 ml of distilled deionized water through the membrane was measured. The same membrane was perfused twice, at a time interval of 3 min. In control experiments, using untreated deionized water, a decrease of permeability in the second measurement was observed (Table), conditioned by the swelling of the connective tissue[5]. In further experiments the water treated by ultrasound (2 or 30 min before) was used for the

	Controls	Water irradiated	
		2 min prior to use	30 min prior to use
Mean % of change of flow time[a]	+19	−21	−22
Number of samples increasing permeability	0	8	7
Number of samples decreasing permeability	17	0	0

[a] Against the value of the first measurement (= 100%).

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second measurement of the flow rate. Distilled, deionized water was treated by ultrasound of 1 W/cm² intensity, frequency 800 kc. Using an irradiation time of 60 sec, the differences in temperature did not exceed $\pm 1°C$, pH ± 0.2. There was also no change of electrical conductivity observed.

The summary of results (Table) indicates a significant increase in permeability of membranes perfused with irradiated water ($P < 0.01$). Unambiguous results, obtained by using deionized water, were not so conspicuous with simple distilled water, especially when irradiated saline solution was used. The oxidizing effect of peroxides on the colloid properties of the connective tissue offers a possible explanation for our findings.

Zusammenfassung. Die Durchlässigkeit des Rattenmesenteriums für demineralisiertes Wasser wird durch Ultraschallbehandlung des Wassers signifikant erhöht.

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Electrolyte Exchange in Regenerating *Dugesia dorotocephala*

The axial polarity of regenerating planarians (*Dugesia dorotocephala* and *D. tigrina*) may be completely controlled by an applied electrical potential gradient[1-3]. Furthermore, the magnitude of the imposed gradient determines the nature of the morphogenetic response. Elucidation of mechanisms involved in this phenomenon requires data pertinent to the electrical resistance of the regenerants. The behavior of the internal electrolyte concentration as a function of the external concentration is theoretically one such important factor.

Electrolyte exchange with the environment was measured by the changes in specific resistance of aqueous media which contained 25 regenerating sections of *D. dorotocephala*. These sections were cut from 5 intact animals, the extreme anterior and posterior pieces being discarded; the sections were washed and transferred to 25 cm³ of medium. Parallel groups of 5 intact animals of equal size served as references and controls. All animals were starved 5 days prior to use. Specific resistances of the media were determined with an A.C. Wheatstone bridge employing an oscilloscope as a null detector and a conventional conductance cell maintained at $23 \pm 0.2°C$ by a water bath. The 8 media were comprised of mixtures of aerated tap water with Ringer's solution or distilled water and ranged from 103.89 to 9616.8 ohm-cm specific resistance. Duplicate 5 cm³ samples were taken at 24 h intervals over a 5 day period, each group of regenerants or intact animals serving for only one measurement. For simplicity, the specific resistances were calculated and expressed as equivalent concentrations of KCl after correction for evaporative loss. The values reported here are the averages of 6 measurements except for the 103.89 ohm-cm medium, which sharply decreased viability.

Figures 1 and 2 show the changes in electrolyte content of the media as a function of time and specific resistance; thus a positive value indicates a loss by the regenerants. The similarity of electrolyte exchange by intact and re-

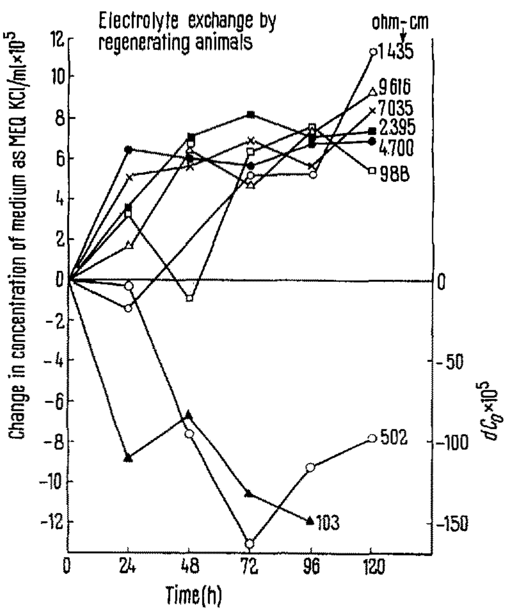

Fig. 1. The change in electrolyte concentration of the medium expressed as MEQ KCl/ml × 10⁵ for media of 8 different specific resistances. Values for 103.89 ohm-cm medium are plotted on the right ordinate, all others on the left.

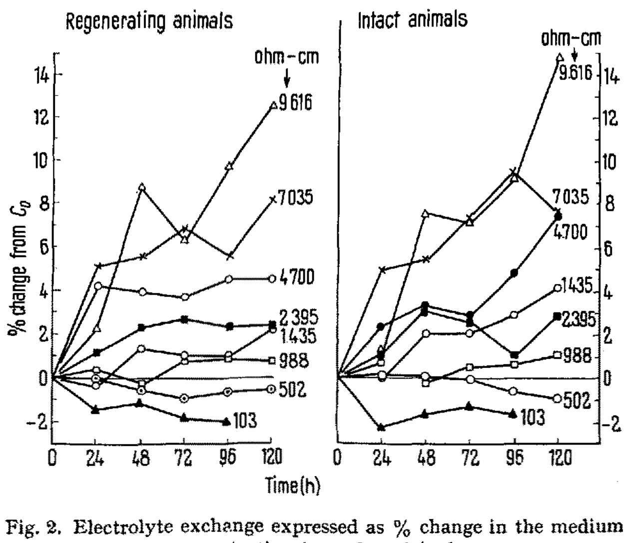

Fig. 2. Electrolyte exchange expressed as % change in the medium concentration from the original.

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