

### Summary

In view of the chronic interstitial nephritis observed in man after years of abuse of phenacetin-containing analgesics, rats were subjected to oral loading-tests with Saridon and its active components. It was not possible, however, to induce interstitial nephritis experimentally. Trials with Saridon will be continued on rats having undergone additional renal loading-tests and in which renal damage has been previously induced.

### Responses of the Middle-ear Muscles to Neuro-muscular Blocking Agents

To facilitate physiological and pharmacological studies on the middle-ear muscles, methods have been developed for recording their contractions under practically isometric conditions. The muscles are stimulated either reflexly from the opposite ear by means of pure tones, or, in the case of musculus stapedius, by

most complete paralysis of the tensor tympani simultaneously with the maximum tonic contraction of the stapedius muscle (Fig. B, 0.4 mg succinylcholine-iodide). Usually the tonic contraction starts while the muscle is still able to respond normally to reflex stimuli. Sometimes, however, almost complete block was seen before the tonic contraction occurred. As a rule the sum of the tonic and the superimposed reflex contractions was somewhat larger than the normal reflex contraction alone. In some experiments no reflex contraction could be seen at the peak of the tonic contraction.

The tonic contractions of musculus stapedius are not prevented by blocking or cutting of its nerve. Decamethonium has the same effect as succinylcholine.

Injection of about 0.1 mg succinylcholine or decamethonium is followed by tonic contraction of musculus stapedius lasting about 1 min. The effect on musculus tensor tympani is considerably shorter.

D-tubocurarine gives no tonic contraction, but blocks musculus stapedius more readily than musculus tensor tympani. On the other hand, this block of musculus stapedius is more easily reversed by succinyl-



Contractions of musculus stapedius (S) and musculus tensor tympani (T) during rhythmic reflex stimulation and after the intravenous injection of succinylcholine-iodide (A: 0.15 mg, B: 0.40 mg). The tracings which read from left to right start at the end of the injection. Time in seconds. The maximum contractions recorded are about 3 g.

electrical stimulation of the facial nerve. The contractions are recorded by means of RCA 5734 transducer tubes carrying small hooks into which the tendons are slipped. In the records shown below the crura of the stapes had been fractured, only the head remaining in contact with the tendon. Similarly the tendon of musculus tensor tympani was left in contact with a part of the malleus, from which the head and the manubrium had been removed. In addition to electrical recording, and in order to distinguish artefacts in the records due to movements of the animal, the muscles were also observed microscopically with a heliometer device. The experiments were performed on rabbits, weighing 2–2.4 kg.

The Figure shows simultaneous records of musculus tensor tympani and musculus stapedius. The contralateral ear was stimulated by means of 1000 cps tone-pips recurring every 2 s, the duration of each pip being 0.2 s. The intensity was adjusted to exceed that required to produce maximum reflex contractions. Pentobarbitone, 30 mg/kg body weight, was used for anaesthesia. At the beginning of record A an injection of 0.15 mg of succinylcholine-iodide in 0.2 ml of saline into the jugular vein had just been finished. The record shows a marked tonic contraction of the stapedius muscle with very little effect on the tensor tympani. In other experiments a similar or larger dose of succinylcholine produced al-

choline than that of the tensor tympani. The de-blocking of the stapedius muscle by succinylcholine is accompanied by a strong tonic contraction.

The reactions of musculus stapedius to succinylcholine and decamethonium resemble those of the extra-ocular muscles described by HOFMANN and LEMBECK<sup>1</sup>.

Details of these and further experiments will be published in *Acta Otolaryngologica*.

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### Zusammenfassung

Unter Benutzung der Röhre RCA 5734 wurde ein isometrischer Myograph zum Studium der Physiologie und Pharmakologie der Mittelohrmuskeln entwickelt. Die Muskeln wurden durch kontra-laterale Tonstöße und im Falle des musculus stapedius durch elektrische Reizung ihres Nerven erregt.

Beim Kaninchen verursachten Succinylcholin und Dekamethonium eine tonische Kontraktion des musculus stapedius, dagegen nicht des musculus tensor tympani. d-Tubocurarin blockiert den musculus stapedius eher als den musculus tensor tympani, ruft aber keine tonische Kontraktion hervor.

<sup>1</sup> H. HOFMANN and F. LEMBECK, *Arch. exper. Pathol. Pharmacol.* 216, 552 (1952).