effect of pH variations on PMN-L chemiluminescence, showed no significant change of CL response in the range of pH from 6 to 8 (unreported data). As could be expected, the in vivo experiments resulted in a less uniform behavior of the CL response, although the inhibitory trend was the rule for the patients who underwent anesthesia by halothane, and inhibition was also the most common response for the cases where ethrane was used. Since GA were shown in vitro to inhibit CL, the inhibition observed in vivo is therefore likely to depend on anesthesia in the first place. Here again we must notice that, because of the time needed for blood transportation and PMN-L separation from whole blood, chemiluminescence was measured $2\frac{1}{2}$ h after the in vivo exposure of PMN-L to halothane or to ethrane.
The lack of uniformity in the extent of inhibition, mainly within the ethrane group, might reasonably be supposed to be due to a partial reversal of the inhibitory effect of GA on chemiluminescence. According to our data, the inhibition of chemiluminescence by GA is more pronounced than the inhibition of phagocytosis by GA, which other authors have shown by means of closely related techniques, i.e. latex ingestion and NBT reduction[11]. Our results on human PMN-L are in agreement with the anesthetic depression of rat lung macrophages that Graham et al.[12] demonstrated, also by a chemiluminescence technique.
An in vivo study designed to assess the time necessary for the restoration of a normal chemiluminescence response after inducement of general anesthesia is currently under way.

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Inhibitory effect of α-α-diphenyl-α-propoxyacetic acid-L-methyl-4-piperidyl ester hydrochloride on the activity of the rat urinary bladder

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Summary. α-α- Diphenyl-α- propoxyacetic acid-l-methyl-4-piperidyl ester hydrochloride(propiverine) significantly decreased the volume-pressure ratio of the rat urinary bladder and suppressed efferent nervous activity of the bladder branch of the pelvic nerve during vesical extension.

α-α-Diphenyl-α-propoxyacetic acid-l-methyl-4-piperidyl ester hydrochloride(propiverine) is a derivative of benzyl acid, and has been reported to exhibit spasmolytic and analgesic effects[1]. A parasympathicolytic effect of propiverine has been suspected, while propiverine attenuated both the acetylcholin- and nicotine-spasm of the isolated ileum of the guinea-pig. In the present experiments, effects of propiverine on the volume-pressure curve of the urinary bladder and pelvic nervous activity were investigated in the rat. Since activation of the detrusor muscle of the rat urinary bladder is due to acetylcholine release from the pelvic nerve endings[2,3], investigation of urine excretion of the rat can be used to investigate the effect of a drug on the parasympathetic effector system.
Male albino rats of the Sprague-Dawley strain, weighing 300–540 g, were used. Animals were anesthetized with urethane, 1 g/kg i.p., before the surgical operation, and a supplemental dose of 150–180 mg of urethane was injected i.v. during experiments, if necessary. The urinary bladder was exposed following midline-incision, and a polyethylene cannula was inserted from the apex. This cannula was connected with a pressure transducer, and simultaneously with an infusion pump by bifurcation of the transducer head. Intravesical pressure was varied by infusing saline through the cannula at a constant rate by means of the infusion pump. Mass discharges of the efferent pelvic nerves (PNA) were recorded with bipolar Pt-electrodes distal to the pelvic plexus. Afferent nervous activity of the pelvic nerve was eliminated by pinching the nerve bundle distal to the recording electrodes. The hypogastric ganglion was ligatured beforehand, in order to avoid sympathetic influence descending through hypogastric nerves. Efferent pelvic nervous activity (PNA) was evaluated semiquantitatively by integrating mass discharges over a 1-sec period. Body temperature of the animal was kept constant, not lower than 36 °C, during experiments, adjusting heat pad

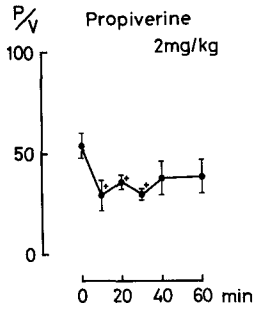

Figure 1. Effect of propiverine on volume-pressure ratio (P/V) of the rat urinary bladder. Means and SE for 4 animals. Propiverine, 2 mg/kg i.v.+, data significantly different from those of control (Student's t-test, $p < 0.05$).

and room temperatures. Propiverine (VEB Sächsisches Serumwerk, Dresden) was resolved with saline by 2 mg/ml, and injected i.v.

For cystometrography, 1.6 ml of saline was infused into the urinary bladder in 1 min. Immediately after starting infusion, vesical pressure began to rise, and reached a plateau in 15-30 sec. Subsequently, at least 1 sequence of rhythmical bladder constriction and urine excretion was observed. Vesical pressure decreased after infusion was stopped. As a parameter of this volume-pressure curve, P/V ratio was employed: P represents vesical pressure of the plateau; V represents the volume of saline infused until vesical pressure reached the plateau level. Figure 1 shows changes in P/V ratio by i.v. injection of 2 mg/kg propiverine. Volume-pressure curve was estimated every 10-20 min after propiverine injection. Mean and SE for 4 animals were demonstrated. Propiverine decreased the P/V ratio significantly at 10, 20 and 30 min after injection (Student's t-test, $p < 0.05$). The maximal decrease in P/V ratio was achieved 10 min after propiverine injection: P/V ratio decreased from 54.8 ± 6.1 to 29.5 ± 7.0. Actual P- and V-values were 38.4 ± 7.3 cmH_2O and 0.8 ± 0.2 ml in the control, and 30.0 ± 6.5 cmH_2O and 1.1 ± 0.1 ml at 10 min after drug application respectively.

In preliminary experiments, saline infusion was carried out at a rate of 0.3 ml/min until the 1st bladder constriction and urine excretion was observed. In the case of this slower infusion rate, infusion time was prolonged by approx. 1.7 times 15 min after propiverine injection, i.e. the saline volume necessary to cause excretion was increased by 1.7 times ($n = 2$).

The effect of propiverine on PNA during the excretory reflex was examined in 4 animals. In these experiments, the urinary bladder was continuously infused with saline by 0.6 ml/min. Vesical pressure above a certain level initiated burst of discharges in the efferent pelvic nerves, and vesical pressure and PNA proportionally increased and decreased during continuous infusion. As shown in figure 2, 2 mg/kg propiverine significantly decreased both vesical pressure and PNA (Student's t-test, $p < 0.05$). This shows that propiverine inhibited the excretory reflex of the urinary bladder.

In the present experiments, the following 2 results were obtained. 1. Propiverine decreased P/V ratio of volume-pressure curve of the rat urinary bladder. 2. Propiverine suppressed efferent nervous activity of the bladder branch of the pelvic nerve during vesical perfusion. As the P/V ratio is supposed to represent both mechanical and reflex properties of the bladder, a decrease in P/V ratio indicates a decrease in the contractile force of the bladder muscle and inhibition of neural components of the excretory reflex. Direct action of propiverine on bladder muscle has recently been proved in the isolated rabbit urinary bladder in vitro[4]. However, a possibility of central action of propiverine cannot yet be considered negligible, because of its inhibitory effects on nicotine-spasm and efferent pelvic nervous activity. Neurotropic action of propiverine will be further investigated. The present experiments showed that propiverine exhibits an inhibitory action on the urine expulsion of the rat, besides its spasmolytic and analgesic effects.

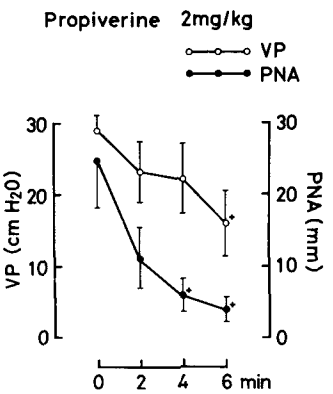

Figure 2. Effect of propiverine on vesical pressure (VP) and efferent pelvic nervous activity (PNA). Means and SE for 4 animals. PNA is shown as mm of recorder deflexion for integrated values. Propiverine, 2 mg/kg i.v.$^+$, data significantly different from those of control (Student's t-test, $p < 0.05$).

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Effects of macrolide antibiotics on barbiturate sleeping time in mice

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Summary. Triacetyloleandomycin and josamycin, when administered to inbred Balb/c mice orally twice daily at a dose of 12.5 or 25 mg per kg over 3 days, were found to increase barbiturate sleeping time significantly. In contrast, erythromycin ethylsuccinate, erythromycin propionate, midecamycin and spiramycin were devoid of any such activity under the same conditions.

The hazards of certain drug interactions with macrolide derivatives have been emphasized previously, particularly concerning ergotamine, the pill, carbamazepine and theophylline on the one hand, and triacetyloleandomycin on the other hand[1]. Available data suggest enzymatic inhibition as a likely mechanism[2]. The status of other macrolide antibiotics is poorly established in this context. In order to provide additional information, we undertook to study the influence of every macrolide marketed in France on barbiturate sleeping time, a good indicator of drug-metabolizing enzyme activities[3].

Methods. Inbred Balb/c mice weighing between 18 and 20 g were purchased from Iffa Credo (France) and randomly used throughout. Each experimental group consisted of 5 male and 5 female animals. Sleeping time was quantified by means of the righting reflex method[4]. In a first series of experiments, mice were given 12.5 or 25 mg/kg triacetyloleandomycin, erythromycin propionate, erythromycin