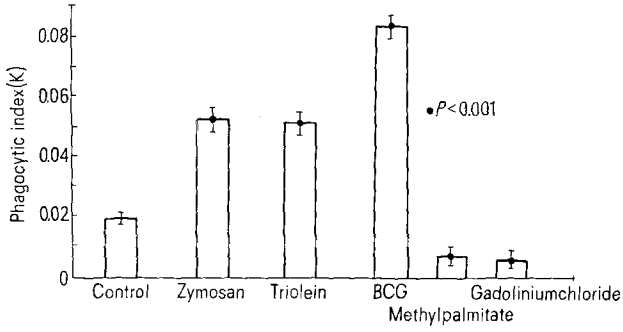
Results. In accordance with other investigations[14-17], zymosan, triolein and BCG markedly increased the granulopectic activity of the RES (Figure). Methylpalmitate[18] and gadolinium chloride caused the same degree of RES depression.

Intense splenic calcification was noted in the controls 4 days after treatment with gadolinium chloride (Table I). Histologically, calcified material was found in the marginal zone and in the red pulp of the spleen.

No calcification was evident in the triolein- or BCG-treated rats, ond only one positive von Kóssa reaction was noted among the animals given zymosan. The cerium chloride-induced fatty infiltration in the rat liver was prevented only by methylpalmitate (Table II).

Discussion. The mechanism through which reticuloendothelial stimulation protects against gadolinium chloride-induced splenic calcification is not yet fully understood. RES stimulation probably alters the distribution of gadolinium chloride. Apparently, the Kupffer cells, not the spleen, play a decisive role in reticuloendothelial stimulation by tumor growth and partial hepatectomy[19-22]. Di Luzio[23], during graft versus host reactions, and Munson et al.[24], during zymosan-induced reticuloendothelial stimulation, noted a depressed splenic uptake and a markedly enhanced hepatic uptake of I^{131}-lipid emulsion.

That the RES participates in lipid metabolism is well-known[25,26]. The prevention by methylpalmitate of cerium chloride-induced fatty livers is in accordance with the investigations of Gaillard et al.[27], who found that the increase of triglycerides and hepatic fatty acids, elicited in rats by ingestion of sodium selenite, ethanol, isopropanol, carbon tetrachloride, ethionine or DDT, is less marked when the RES is partially blocked by ethyl stearate. However, further investigations are needed to determine why gadolinium chloride did not protect against cerium chloride-induced fatty livers[28].



Reticuloendothelial activity in rats treated with zymosan, triolein, BCG, methylpalmitate or gadolinium chloride.

Résumé. Chez le rat, la calcification de la rate produite par le chlorure de gadolinium peut être prévenue par des activateurs de SRE tels que le zymosan, la trioléine et le BCG. Le chlorure de cérium produit dans le foie une dégénérescence graisseuse empêchée par le méthylpalmitate qui est un inhibiteur du SRE.

G. Lazar[29]

Institut de médecine et de chirurgie expérimentales, Université de Montréal, C.P. 6128 Montréal 101 (Quebec, Canada), 7 August 1972.

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[29] Present address: Medical University of Szeged, Institute of Pathophysiology, Szeged (Hungary).

The Effect of Semicarbazide Pretreatment on the Depressant Action of Barbiturates

The depressant action of barbiturates on spinal synaptic activity is well studied. Transmission across both monosynaptic and polysynaptic reflex arcs is depressed[1], while the amplitude and duration of the segmental dorsal root potential (DRP) is increased after smaller doses, and the time for half-decay further prolonged by larger doses[2]. The contribution of the barbiturate-induced increase in DRP to the depression of the ventral root discharge is difficult to assess. Furthermore, it is not known whether the action of barbiturates is mediated through some spinal inhibitory substance or whether it results from a direct action on neuronal elements. Since γ-aminobutyric acid (GABA) is present in the spinal cord[3] and exerts a potent depressant action on spinal neuronal activity when applied microelectrophoretically[4], while depolarizing afferent presynaptic terminals when added to the perfusing medium[2], the effects of pentobarbital (Nembutal) on spinal transmission were examined after depletion of GABA by semicarbazide, a compound which blocks the synthesis of this inhibitory amino acid[5].

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Depression of the MSR and increase in the DRP by pentobarbital

Dose of pentobarbital (mg/kg)	Semicarbazide-treated cats MSR[a]	DRP	Saline-treated cats MSR[a]	DRP
10	22 ± 7 (6)	No effect (3) or mild increase in amplitude (3)	31 ± 6 (8)	Increase in amplitude and/or duration (8)
20	10 ± 8 (6)	No effect (6)	12 ± 7 (4)	Increase in duration (4)

[a] The depressed MSR is expressed as mean % of control followed by the standard error and number of experiments in parentheses. The size of the MSR $4^1/_2$ h after semicarbazide or saline is taken as control.

After cannulating the trachea and ligating carotid arteries of cats initially anesthetized with ether, the spinal cord was severed at the level of the atlanto-occipital junction. Ether was then discontinued and the cats immediately placed under artificial respiration, with end tidal CO_2 levels controled at 3.5–4%. The brain was made ischemic by local pressure applied on the vertebral arteries for 5 min. The lumbosacral cord was exposed, the dura sectioned, and ventral L_6, L_7, and S_1, and all contralateral dorsal and ventral roots were cut. The exposed tissues were covered with warm mineral oil, the temperature of which was maintained at 37 °C thermostatically. The ipsilateral hamstring nerves were dissected out, crushed distally, and placed on platinum hook electrodes for stimulation (12 c/min) in a pool of warm mineral oil. All other leg nerves were sectioned. Reflex transmission was recorded in ipsilateral ventral L_7, while the DRP was recorded from a dorsal L_6 rootlet, with the time constant of the preamplifier set at 1 sec.

The effects of i.v. administration of semicarbazide (200 mg/kg) on spinal cord potentials have already been described[6,7]. The most pronounced effect was the gradual depression of the DRP (specifically DRV), which was reduced in area to below 20% of control size and sometimes completely blocked within $4^1/_2$ h of drug administration. The ventral root discharge was usually facilitated, as shown by the increase in size of the monosynaptic (MSR) and polysynaptic (PSR) responses in 4 out of 6 cats. Pentobarbital was administered i.v. 270 min after semicarbazide, at a time when GABA has been shown to be completely depleted from the spinal cord[6]. In all 6 experiments, it resulted in immediate depression of the MSR and PSR. A dose of 10 mg/kg depressed the MSR to 22 ± 7% of control size, while 20 mg/kg depressed it to 10 ± 8% (Table). In 3 of these experiments, pentobarbital (10 mg/kg) failed to increase the DRP, while in the remaining 3 experiments, it mildly increased its amplitude. With larger doses (20 mg/kg or more), it uniformly failed to prolong its duration. All these effects were obtained irrespective of the strength of stimulation of the hamstring nerve (3- and 12-times threshold).

In control experiments where the cats were given saline in place of semicarbazide, the administration of pentobarbital (10-20 mg/kg) $4^1/_2$ h later resulted in depression of the MSR and PSR (Table), a well-defined increase in the amplitude of the DRP after smaller doses, and a definite prolongation of its duration after larger doses (20 mg/kg).

Thus it can be seen that pentobarbital is at least equally depressant in the presence or absence of GABA. Its depressant action on ventral root discharge, therefore, is not mediated, even partly, by this inhibitory transmitter candidate. It probably results from a direct effect on synaptic elements, decreasing the release of the primary afferent transmitter in smaller doses[8,9], and reducing the excitability of motoneuronal membranes in larger doses[10,11].

Another interesting conclusion is that the depressant action of pentobarbital on ventral root discharges can be dissociated from its ability to increase primary afferent depolarization, since in some experiments, depression of reflex transmission in the ventral root occurred in the absence of a concomitant increase in the size of the DRP[12].

Résumé. Le pentobarbital fait diminuer la transmission à travers le relais monosynaptique de la moelle épinière chez les chats décapités dépourvus de GABA sous un traitement au semicarbazide, et ceci par un degré équivalent à celui des expériences de contrôle.

N. R. BANNA

School of Pharmacy, American University of Beirut, Beirut (Lebanon), 15 November 1972.

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Phenobarbital Specific Antisera and Radioimmunoassay

Antibodies developed against drug haptens have been used in immunoassays of drugs in biological fluids[1,2]. We now report the procedures for developing an antibody which is highly specific to phenobarbital (5-ethyl-5-phenylbarbituric acid) and can be used in radioimmunoassay to detect picomole levels of this drug in biological fluids. The significant difference in the specificity of this antibody and that of antibody produced by SPECTOR and FLYNN[2] is of particular interest.

The barbiturate-protein conjugate was made by dissolving 1.25 g of 5-phenyl-5-(4-aminobutyl) barbituric acid hydro-chloride containing a small amount of