cholestérol de l'aorte est en moyenne de 783 ± 70 mg/100 g de poids frais chez les Fauves mais s'élève à 1172 ± 82 mg chez les Néozélandais, les lésions athéromateuses étant également plus intenses (Figure 2). Concernant ces lésions, il est à souligner que l'analyse biochimique des vaisseaux fournit des résultats en tous points comparables à ceux de l'examen anatomopathologique.

Ainsi donc, aussi bien en ce qui concerne les troubles de la circulation des lipides que les lésions artérielles, les lapins Néozélandais se révèlent remarquablement plus sensibles que les Fauves.

Discussion. Nous avons vérifié que l'absorption intestinale du cholestérol était analogue dans les deux races de lapins. Par conséquent, les raisons de ces différences doivent être recherchées au niveau d'autres tissus.

En premier lieu, nous avons confirmé chez le Lapin soumis au cholestérol l'instauration progressive d'une hypothyroïdie nette. Or, il se trouve que cette hypoactivité est bien plus accusée chez les lapins Néozélandais. Il est possible que la gravité plus grande des lésions artérielles soit en relation avec cette constatation, puisqu'il est bien établi que l'hypothyroïdie favorise l'athérosclérose.

Une autre hypothèse peut également être envisagée. Les lipides qui sont à l'origine de l'hyperlipémie proviennent non seulement des réserves adipeuses mais également de la moelle osseuse, surtout au début du traitement (MARQUIE[1]). Or, nous avons observé également à ce niveau les signes d'une vive stimulation érythropoïétique qui se traduit d'ailleurs au niveau du sang par une élévation des réticulocytes, et une hyperlymphocytose (MARQUIE et al.[3]). Toutes choses égales par ailleurs, l'ensemble de ces manifestations est nettement plus accusé chez les lapins Néozélandais chez lesquels la mobilisation lipidique est précisément la plus intense. Bien qu'une relation de cause à effet soit encore à démontrer, nous estimons que cette relation entre la stimulation du système hématopoïétique et la mobilisation lipidique est importante à considérer et pourrait éclaircir la différence de sensibilité des deux races de lapins soumis au même régime athérogène.

Zusammenfassung. Am Beispiel von experimentell erzeugten Atheromen beim Kaninchen zeigen sich in Bezug auf den Stoffwechsel charakteristische Rassenunterschiede. Variable Dosis von Cholesterol erzeugt bei der Neuseeländer Rasse, verglichen mit der Fauves-Burgunder-Rasse, biochemisch wie auch histologisch wesentlich stärkere Hyperlipaemie, Fettinfiltration der Leber und arterielle Läsionen.

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A Novel Monoquaternary Neuromuscular Blocking Agent

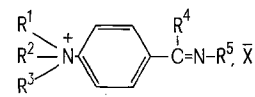
We have for many years sought a clinically useful muscle relaxant which would be both short acting and readily reversible. After extensive structural and stereochemical studies of steroid bisquaternary ammonium salts[1-3], we investigated the nature of the basic head in other *bis*-quaternary and related dibasic salts[4,5]. Concurrent work in the steroid field having shown that 2 quaternary centres were not essential for potent curarising properties[6], we prepared and examined pharmacologically other types of monoquaternary salts.

We now report that *p*-dimethylaminophenyl heptyl ketone thiosemicarbazone ethiodide (M&B 15,944), selected from a series of functional derivatives of general formula (I), appears to possess the desired properties.

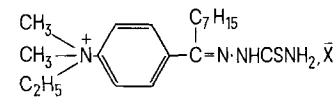
M&B 15,944 has been examined both as the iodide and as the more water-soluble chloride M&B 15,944 A. All doses given refer to the cation.

The neuromuscular blocking activity of the compound has been studied in the sciatic tibialis, sciatic soleus or sciatic gastrocnemius muscle preparation of the anaesthetised cat, dog, rhesus monkey, baboon and chicken (Table). In all species examined it produced a short acting neuromuscular blockade which could be reversed by anticholinesterases or by a tetanus applied to the nerve. Further evidence of its competitive mode of action was provided in experiments in the chloralose-anaesthetised cat, in which M&B 15,944A blocked the twitch caused by close intra-arterial injection of acetylcholine, and its neuromuscular blocking action summated with that of drugs with a similar type of action, e.g. D-tubocurarine. M&B 15,944 failed to cause contracture of the gastrocnemius muscle and caused flaccid paralysis when injected intravenously into the conscious chick. In contrast, suxamethonium produced a spastic type of paralysis in the chick.

M&B 15,944 has been found to lower the blood pressure in the anaesthetised cat, dog and chick but not in the rhesus monkey or baboon. This hypotensive action is not due to an α-receptor blocking action or to histamine release. M&B 15,944 was, however, found to possess significant ganglion-blocking activity which may account for the falls in blood pressure seen in some species.



(I)



M&B 15,944, X = I

M&B 15,944 A, X = Cl

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The neuromuscular blocking activity of M&B 15,944 in various species compared with that of suxamethonium bromide

Species	Preparation	M&B 15,944		Suxamethonium	
		i.v. ED50 (mg/kg)	Duration at ED50 (min)	i.v. ED50 (mg/kg)	Duration at ED50 (min)
Cat	Sciatic nerve tibialis muscle	0.97 (10) [a]	3.5		
		1.1 (5) [b]	3.0	0.013 (4)	4.3
	Sciatic nerve soleus muscle	1.8 (5) [b]	5.3	0.020 (4)	4.3
Dog	Sciatic nerve tibialis muscle	1.43 (4) [a]	7.5	0.02 (4)	5.6
Rhesus monkey	Sciatic nerve tibialis muscle	0.44 (2) [b]	4.0	—	—
	Sciatic nerve soleus muscle	0.28 (2) [b]	2.5	0.35 (3)	4.0
Baboon	Sciatic nerve tibialis muscle	0.34 (3) [b]	3.5	0.21 (1)	1.7
Chicken	Sciatic nerve gastrocnemius muscle	1.37 (3) [a]	5.3	—	—

Effective doses (ED50) are those required to reduce to 50% the heights of the muscle twitches produced by stimulation of the motor nerve in the anaesthetised animal. The compound was used either as the chloride or iodide. Doses refer to the cation. Figures in () refer to the number of experiments. [a] Iodide used. [b] Chloride used.

Résumé. Le M&B 15.944 (éthiodide de *p*-diméthylaminophényl heptyl cétone thiosémicarbazone) est un curarisant dont la brève durée d'action est comparable à celle de la succinylcholine chez divers espèces y compris le singe. Le méchanisme du blocage neuromusculaire provoqué par le M&B 15.944 est compétitif.

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Effect of Ketamine Hydrochloride on Oxygen and Glucose Uptake by Brain Tissue in vitro

Ketamine hydrochloride (CI-581) is a dissociative anesthesic agent which was introduced by DOMINO et al.[1]. There are contradictory data about the effect of this drug on cerebral utilization of oxygen in vivo. KREUSCHER et al.[2] reported a decrease of brain oxygen uptake in dogs treated with Ketamine hydrochloride, whereas DAWSON et al.[3] found that the drug increased the oxygen uptake, an effect which was abolished by prior administration of Thiopental. We have studied the effect of ketamine hydrochloride on the oxygen and glucose utilization by rat brain slices and brain homogenates. Since the depressing action of brain oxygen uptake elicited by some anesthesic agents is more evident when the tissue respiration has been stimulated by high potassium concentrations (GHOSH and QUASTEL[4]; TAMARIT[5]). We also studied the effect of ketamine hydrochloride at low and high potassium concentrations.

Materials and methods. Brain slices and brain homogenates were prepared from adult male albino rats (150–200 g body wt.) killed by decapitation. The slices were obtained as described by MCILWAIN and BUDDLE[6] and were incubated in Krebs-Ringer phosphate medium (pH 7.4), which contained 10 m*M* glucose and 5 m*M* or 100 m*M* potassium. Whole brain homogenates were prepared at 2–4 °C in a Potter-Elvehjen homogenizer, mixing 1 g tissue samples with 9 ml of a solution containing 0.25 *M* sucrose and 0.1 *M* phosphate buffer (pH 7.4).

Oxygen utilization at 37 °C was determined by direct manometric technique (UMBREIT et al.[7]), using a conventional Warburg apparatus with air as gas phase. Glucose uptake was estimated by measuring the glucose concentration in the medium at the end of incubation with a glucose oxidase method (SOLS and DE LA FUENTE[8]). Student's *t*-test was applied for the statistic significance of the data (SNEDECOR[9]).

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