# ROYAL ACADEMY OF MEDICINE IN IRELAND

A Meeting of the Biological Sciences Section was held in the Royal College of Physicians, 6 Kildare Street, Dublin on Friday, 15th December, 1967.

## ACTION OF TRAGACANTH ON ASCITES TUMOUR CELLS IN VITRO

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Tragacanth is known to inhibit mitosis in ascites tumour cells without actually penetrating into the cell. PAS staining has shown that this inhibition is associated with attachment to the cell surface of long branched particles of mucopolysaccharide. Tragacanth rendered non-inhibitory by boiling gives a different, less specific staining picture. (Roe, 1959, Galbraith, Mayhew & Roe, 1962). The mode of action is unknown, but could be through effects on transport of essential substances. The effects of tragacanth on ascites cell K and Na are being examined by us and the *in vitro* findings are described here.

With unwashed suspensions of ascites cells, tragacanth is shown to cause gross imbalance of K/Na equilibrium. No such effect occurs with heat-inactivated (non-inhibitory) tragacanth. Similar effects were found with Ringer-washed cells. Under the later conditions, due to absence of ascitic fluid, the typical combination of tragacanth with the cell surface does not take place and there is no difference in PAS staining between the inhibitory form and the non-inhibitory control (Roe, personal comm.), both forming a non-particulate coating round the cell. When ascitic fluid is absent it appears therefore that K/Na estimations, unlike PAS staining, can still sharply differentiate between these two forms of tragacanth.

*References*

Roe, E.M.F., (1959). Nature, 184, 1891.
Galbraith, W. Mayhew, E. and Roe, E.M.F. (1962). *Brit. J. Cancer*, XVI, 163.

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## EXPERIMENTAL SOFT TISSUE CALCIFICATION

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Selye* (1962) showed that the injection of lead acetate subcutaneously in rats resulted in the formation of a calcified plaque at the site of the injection.

In this study similar calcified plaques have been found after the injection of lead acetate subcutaneously in rats and in mice, guinea pigs, golden hamsters, rabbits and chickens. In mice and hamsters 100 $\mu$g., in guinea pigs 200 $\mu$g., in rabbits 300 $\mu$g., and in chickens 350 $\mu$g., of lead acetate were required to elicit this response.

The progress of plaque formation was followed in mice. Lead salts were found at 5 and 60 minutes after injection. After 5 hours phosphate ions were present and a minimal amount of calcium was found while traces of the injected salt remained. After 24 hours phosphate and calcium ions were readily demonstrated while the injected lead salt had almost disappeared from the site. After 6 days the chemical content of the plaque was unaltered and multinucleate macrophages were present around its periphery. Plaques persisted up to 70 days after injection.

Marked degranulation of mast cells was not initially found in the vicinity of the injection but degranulation of mast cells in the immediate vicinity of the plaque occurred after 5 hours and persisted.

*Selye, H.; Tuchweber, B.; Gabbiani, G. (1962) . "Calcinosis Induced by Lead Acetate". *J. Pharmacol.*, 138, 131–138.

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## THROMBUS FORMATION ON CHARGED WIRE IN THE RAT VEIN

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Earlier workers had suggested a possible relationship between the potential of an electrode in blood and the amount of thrombus deposited on it[1]. This was tested by inserting charged platinum and aluminum wires into the rat vena cava. The wires were maintained at potentials from +400 to −400 mV NHE for platinum and −400 to −1 volt-NHE for aluminum. Eight determinations of thrombus weight were carried out for each 100 mV step in the platinum series. Two were carried out at each in the aluminum series. The

[1]Sawyer, P. N. and Plate, J. W., *Amer. J. Physiol.*, 175, 103, 1953.

wires were left in situ for an hour, then removed, and the thrombus weighed to the nearest tenth of a milligram.

No correlation between thrombus weight and electrical potential was observed. In addition growth of a thrombus on a platinum wire at +400 mV NHE was studied. Here, thrombus weight was found to increase with time up to one hour.

The results indicate that thrombus formation on platinum wire in rat vein is a random phenomenon, independent of charge.

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## A METHOD FOR THE DIRECT ESTIMATION OF TOTAL SERUM THYROXINE

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Serum is deproteinized using 95% Ethanol. The $T_4$, thus released from protein binding, is quantitated by its competition with a fixed amount of $T_4$ $125^1$ for binding sites on a fixed amount of Thyroxine Binding Globulin.

As well as providing a direct measurement of circulating $T_4$, the method is free from the effects of usual contaminants which invalidate the Protein Bound Iodine (P.B.I.) estimation.

Subjects were classified as Hypothyroid, Euthyroid, and Hyperthyroid by the usual clinical criteria. The normal range for clinically Euthyroid subjects was 3.3—8.6 $\mu$g/100 ml Thyroxine Iodine.

Agreement with clinical status in a group of 129 patients was 97.2% in Euthyroidism, 100% in Hypothyroidism and 91.4% in Hyperthyroidism.

Correlation with clinical status of $T_3$ uptake by Sephadex gel, in vivo Radioiodine studies, and Thyroxine Iodine, was investigated in a group of 40 patients. Both Sephadex and Radioiodine studies agreed with clinical status in 72.5% of cases while Thyroxine Iodine agreed in 87.5%.

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## THE PRODUCTION OF INTERMITTENT BRADYCARDIA BY SOME ORGANOCHLORINE INSECTICIDES AND THEIR RELATED COMPOUNDS

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Some but not all organochlorine compounds produce intermittent cardiac slowing which precedes the onset of total convulsive episodes in rats anaesthetised with urethane. Dieldrin, aldrin, endrin, isodrin, morphine and picrotoxin all produced intermittent bradycardia which preceded total convulsive activity. There was however fibrissal movement prior to and concomitant with the onset of bradycardia. Other chlorinated hydrocarbon insecticides lindane, chlordane, toxaphene, and heptachlor, have been shown to produce intermittent bradycardia but in these cases the phenomenon was not discrete but part of the convulsive episode.

The phenomenon appears to be mediated by the vagus nerve since section of the left and right branches of this nerve prevents the onset of bradycardia. The phenomenon is not seen in rats premedicated with atropine which affords further evidence of the cholinergic nature of the event.

The response is not part of a simple cardiac reflex phenomenon from the carotid arteries or the carotid bodies although the possibility of a reflex change in heart rate induced by changes in the stretch sensitive receptors of the aortic arch has not been completely discounted. However the fact that rats anaesthetised with sodium pentobarbitone do not show bradycardia gives further evidence of the probability that the insecticides evoke central activation of the vagus nerve. The slowing is not due to any change in the conduction system of the heart, it appears to be due to a change in the rate of firing of the "pacemaker" of the sino-auricular node. There is no evidence of changes in the electrical complex of the ECG. However, there is some small amount of evidence that these compounds are not acting upon the vasomotor area of the medulla but in an area probably rostral to the medulla in the region of the Cingulate Gyrus.

An attempt to show that the derived epoxides of aldrin and isodrin were the causal agents of the bradycardia has not been proved, but this suggestion has not been completely excluded.