Conventional seven-barrelled micro-pipettes are inserted through holes in the pressor foot 2 to 3 mm caudal to the obex, and escape of C.S.F. through these holes helps to keep the brain moist and warm. Extracellular action potentials are recorded whilst GABA, glycine and various antagonists are applied to single neurones (see Hill, Simmonds & Straughan, 1972), and stable recording conditions are maintained for two or three hours without difficulty.

Only spontaneously firing neurones are used, in order to avoid the type of over excitation produced by a combination of picrotoxin and glutamate described by Galindo (1969). As neurones are not physiologically identified it is possible that they are not exclusively in the cuneate nucleus. However, the pharmacological picture of sensitivity to GABA, glycine and the various antagonists is consistent throughout the population studied.

The preparation and on-line analysis of action potential data will be demonstrated.

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Pharmacology of the neuronal excitation and inhibition induced by an acute seizure focus in feline cortex

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When sodium benzyl penicillin is applied topically to the cerebral cortex, it produces an acute seizure focus characterized by large amplitude spikes and waves in the electrocorticogram (E.Co.G.) and accompanied by paroxysmal activity of single neurones (Matsumoto & Ajmone-Marsan, 1964; Clarke & Hill, 1972). Microinjection of a concentrated penicillin solution into the grey matter produces a more discrete focus so unit activity in and around the area can be mapped with precision (Clarke, Hill & Straughan, 1972). Some features of this preparation are demonstrated.

A sharp E.Co.G. spike with a total duration of 20 to 50 ms is recorded from the focus via the microinjection cannula. This spike is used to trigger a small computer and also the sweep of a storage oscilloscope, so that unit activity time-locked to paroxysmal events in the focus can be studied. Neurones in the immediate vicinity of the focus and also in homotopic areas of the opposite hemisphere have been examined using standard microelectrophoretic techniques and extracellular recording. A typical response shows a burst of action potentials (about 20 ms in duration) synchronous with the E.Co.G. spike, followed by a period of inhibition (lasting about 200 ms) before the firing pattern returns to normal. Thus, in addition to providing a model of epileptiform events, this preparation provides an effective endogenous excitatory and inhibitory input to cortical neurones.

Although the focally evoked burst of action potentials looks similar in all areas, there are pharmacological differences. Thus, within a radius of about 2 mm of the microinjection, the firing is resistant to GABA, whereas evoked firing in more distant areas is readily depressed by GABA in characteristic fashion. The inhibitory pause, best seen relatively distant to the microinjection, looks similar to the inhibition induced by electrical stimulation of the cortex. However, only the latter inhibition is reduced

by the systemic injection of bicuculline (Clarke *et al.*, 1972). Further investigation of these phenomena is in progress.

The use of a small computer for on-line data analysis will also be demonstrated.

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Gas chromatography – mass spectrometry for the identification of barbiturate metabolites

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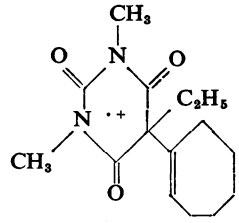
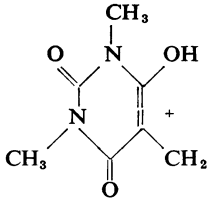
Combined gas liquid chromatography/mass spectrometry has been used previously in the study of drug metabolism (Hammer, Holmstedt, Lindgren & Tham, 1969). The sensitivity of the technique is greatly enhanced when the mass spectrometer is used as a specific detector for certain fragment ions, a procedure called mass fragmentography (Hammar, Holmstedt & Ryhage, 1968). The present demonstration makes use of this technique in the study of the metabolism of heptabarbitone in man.

A single dose of heptabarbitone (400 mg) was taken by a volunteer and urine collected in 8 h batches. Aliquot portions (100 ml) were extracted and processed by methods previously described (Gilbert, Millard, Powell, Whalley & Wilkens, 1972). The extracts from a blank urine sample and each of the 8 h samples were run on a Pye 104 gas chromatograph fitted with a flame ionization detector. The instrument was fitted with a 9 ft 1% QF1 column and was operated isothermally at 200° C for 5 min, then programmed at 6° C/min to 250° C.

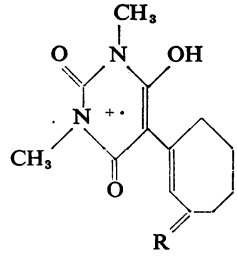
Fig. 1 Mass spectroscopic ions.



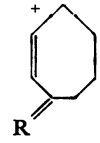
Parent methylated heptabarbitone m/e 278



Fragment ion present in all 5-ethyl substituted barbiturates m/e 169.



R=H,OH m/e 266
R=O m/e 264



R=H,OH m/e 111
R=O m/e 109