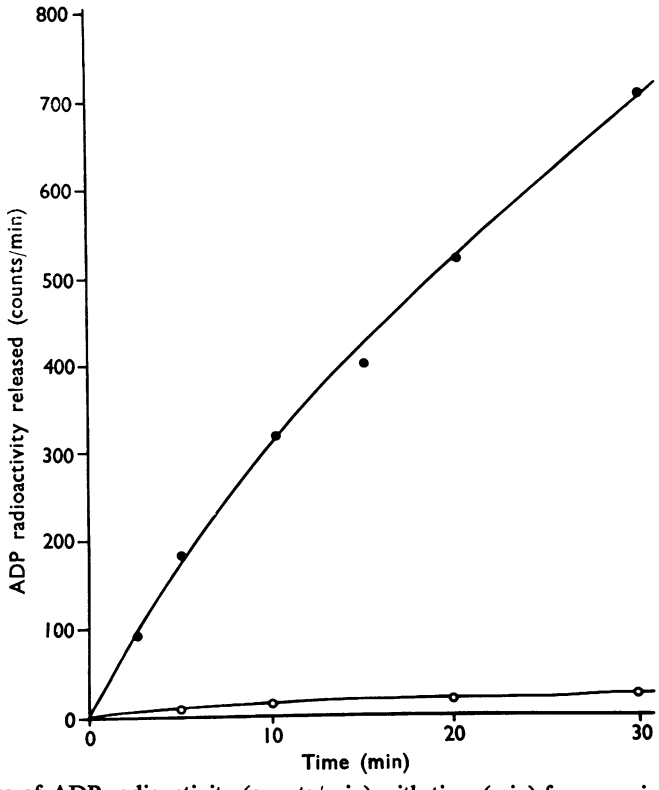

FIG. 1. Release of ADP radioactivity (counts/min) with time (min) from a micropipette (resistance 20 MΩ) filled with 10^{-2}M tritiated ADP, without (○——○) and with (●——●) a current of 300 nA.

A micropipette and the electrode were immersed in 0·5 ml saline in a counting vial. The micropipette was inclined only 20° above the horizontal to minimize bulk outflow. When a negative potential was applied to the pipette, radioactivity appeared in the saline and increased linearly with time for at least 20 min; without the current the release of radioactivity was minimal (Fig. 1). In a given time, for example, 10 min, the release was proportional to current up to at least 300 nA.

With 300 nA, ADP was released at about 2×10^{-14} mol/s. Such a current produced platelet thrombi in normal venules within 5 s. The micropipette tip is less than 5 μM from the vessel wall, so that the concentration of ADP *outside* the wall at least may be quite high.

REFERENCES

BEGENT, NICOLA & BORN, G. V. R. (1970a). Quantitative investigation of intravascular platelet aggregation. *J. Physiol. Lond.*, in the Press.

BEGENT, NICOLA & BORN, G. V. R. (1970b). Growth rate *in vivo* of platelet thrombi, produced by iontophoresed ADP, as a function of mean blood flow velocity. *Nature, Lond.*, in the Press.

BORN, G. V. R. (1962). Aggregation of blood platelets by adenosine diphosphate and its reversal. *Nature, Lond.*, **194**, 927–929.

DULING, B. R., BERNE, R. M. & BORN, G. V. R. (1968). Microiontophoretic application of vasoactive agents to the microcirculation of the hamster cheek pouch. *Microvascular Res.*, **1**, 158–173.

Interaction between anticonvulsant drugs and vitamin D

A. RICHENS and D. J. F. ROWE, *Division of Clinical Pharmacology and Department of Neurophysiology, St. Bartholomew's Hospital, London E.C.*1, *and Metabolic Unit, University College Hospital, London W.C.*1

TABLE 1. *Effect of pretreatment with phenobarbitone on the toxic action of calciferol in rats*

Group	% change in body weight on calciferol	Heart weight (% of body weight)	Kidney weight (% of body weight)	Kidney calcium (mM/kg)	Serum calcium (mM/100 ml)	Serum phosphorus (mg/100 ml)	Serum alkaline phosphatase (KAU/100 ml*)
A–B	−15·3±1·7	+0·01±0·006	+0·16±0·03	+7·7±3·2	+2·8±0·4	+0·2±0·4	−9·1±0·9
C–D	−27·0±1·6	+0·04±0·008	+0·25±0·04	+39·3±8·8	+4·8±0·4	−2·1±0·5	−3·0±0·7

Treatment: Group A=Phenobarbitone+calciferol. Group B=Phenobarbitone+arachis oil. Group C=Distilled water+calciferol. Group D=Distilled water+arachis oil.

The figures given are the differences of the means±S.E. of the groups pretreated with phenobarbitone (A–B) and the groups which received distilled water (C–D).

* King-Armstrong units/100 ml.

A survey of 160 adult epileptic patients in a long-stay residence has demonstrated a 22·5% incidence of mild hypocalcaemia, which was related to the daily dose and number of major anticonvulsants received and particularly to use of pheneturide and primidone (Richens & Rowe, unpublished). The tendency for a raised liver alkaline phosphatase isoenzyme to be related to hypocalcaemia suggested that these drugs may be interfering with calcium metabolism by an action on the liver, perhaps by disturbing vitamin D metabolism. This hypothesis has been tested in rats. Two of four equal groups of male albino rats (seven in each group) were given phenobarbitone (1 mg/ml) in their drinking water for 10 days, while the remaining two groups received distilled water. One phenobarbitone-treated group and one control group were given 40,000 units of calciferol in arachis oil daily by mouth for 8 days, and then killed. Their livers, kidneys and hearts were removed and weighed separately. Serum calcium, phosphorus and alkaline phosphatase, and the calcium content of the ashed kidneys were estimated. Satisfactory liver enzyme induction was demonstrated by a liver weight 44% higher in the phenobarbitone-treated ($P<0·001$). Table 1 summarizes the results.

A comparison of the differences of the means revealed that phenobarbitone (*a*) reduced the weight-loss caused by calciferol ($P<0·001$), (*b*) reduced renal calcinosis ($P<0·01$), (*c*) reduced the rise in serum calcium ($P<0·01$) and (*d*) prevented the fall in serum phosphorus ($P<0·005$). In addition, phenobarbitone appeared to lessen the increase in heart weight ($P<0·01$) and kidney weight ($P<0·05$), but these were probably relative increases due to the loss of body weight. The reduction in alkaline phosphatase produced by calciferol was not significant but phenobarbitone potentiated this effect ($P<0·01$). The mechanism of this action is uncertain. The results of these experiments support the hypothesis that phenobarbitone interferes with calciferol metabolism possibly by enhancing its liver degradation.

One of us (A. R.) was supported by a Wellcome Research Fellowship.

Pharmacologically active substances in malignant ascites fluid

JENNIFER A. C. SYKES (introduced by K. HELLMANN), *Cancer Chemotherapy Department, Imperial Cancer Research Fund, London WC2A 3PX*

There is a low degree of peritoneal inflammation of uncertain origin in mice bearing various types of ascitic tumours. Prostaglandins of the E series are present in carrageenin-induced inflammatory exudate (Willis, 1969) and in medullary carcinoma of the thyroid and its venous effluent (Williams, Karim & Sandler, 1968). Fluid from malignant ascites tumours has now been investigated for the occurrence of prostaglandins and other pharmacologically active substances.

Mice (C3H/He) were inoculated intraperitoneally with 0·2 ml ascitic fluid (BP8/P_1). Seven days later about 0·7–5 ml of peritoneal fluid from each of fifteen to twenty inoculated mice was aspirated, combined and collected in polythene centrifuge tubes. Total fluid volume was measured and cell counts were made. The fluid was centrifuged at 3,000 *g* for 10 min and the supernatant was decanted off and stored at −20° C until required.

The crude supernatant had smooth muscle stimulating activity when assayed on the rat stomach strip (Vane, 1957), chick rectum (Mann & West, 1950) and the rat