Results. Generally, it was found that electrodes made according to the above procedure were of relatively low impedance. The silver paint poles were of somewhat higher impedance than the steel silver solder coated core. For example, in a direct current system and using isotonic saline as a conductor, impedance of the steel core pole was about 3,000 ohms while that of the silver paint pole was about 30,000 ohms. This may appear to be high; however, in animal bio-electric systems (*in vivo*) the characteristics are such that passage of current and voltage indicated a much lower impedance than that found in D.C. systems.

Deep electroencephalographic tracings were made from bi-polar silver paint electrodes implanted chronically in the anterior hypothalamus, posterior hypothalamus and the basal-anterior mesencephalic reticular formation of the cat (Fig. 2). Tracings were also taken from the thalamus by a multipolar electrode (4 separate poles) (Fig. 3). One notes that the recordings are stable and free of electrode "noise." Further the electroencephalograph must be attenuated at the pre-amplifier to reduce the sensitivity of the electrode.

Using both bi-polar and multi-polar electrodes in stimulating and recording sites of the brain stem, oscillographic recordings were made in the vestibular nuclei, the medial longitudinal fasciculus, the sulco-marginal bundle and anterior gray horns of the spinal cord. Stimulating voltages of from 0.1 of a volt to 1.0 volt were used in most cases. Clear cut potentials were easily obtained at the above low voltages in the vestibulo spinal system (Fig. 3).

Electrodes in the foregoing positions have been implanted chronically in cats and left in position for up to 5 months without dramatic changes in either the electroencephalographic or oscillographic tracings. Changes do occur in the above recordings for about 2 weeks following implantation. This is probably due to a chemical change on the exposed silver recording and stimulating points thru action of extracellular fluid, because a light film of blackened silver could be scraped from the recording and stimulating points on removal from the brain.

Acute short term experiments have been performed with these electrodes with equally good results.

Summary. A new type of multi-polar stimulating and recording electrode was developed to answer certain technical difficulties arising through use of standard type electrodes. This relatively low impedance electrode was constructed by using silver "printed circuit" paint over coats of insulating material without greatly increasing the diameter of the electrode core. Both acute and chronic bio-electric experiments were carried out employing the above electrodes giving good amplitude, stable electroencephalographic and oscillographic records from the central nervous system.

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Passage of Barbital into Cerebrospinal Fluid.* (25610)

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Previous studies have shown that barbital given intravenously passes slowly into the brain(1,2). In this report, the latter study was extended to include observations in dogs on passage of barbital into the cerebrospinal fluid.

Methods and materials. Barbital was determined by the method of Giotti and May-

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TABLE I. Sodium Barbital 100 mg/kg Intravenously to Dogs.

Time, min.	Wt, kg	Plasma, mg/l*	Brain, mg/kg*	CSF, mg/l*	Conc. ratio Brain plasma	Conc. ratio CSF plasma
3	10.2	189	52	27	.27	.14
"	10.8	"	44	12	.23	.06
"	10.0	169	27	13	.16	.08
9	11.4	162	51	35	.31	.22
"	13.2	130	58	38	.45	.28
30	23.0	151	93	64	.62	.43
"	24.5	141	99	68	.70	.48
"	19.5	107		43		.40
60	10.0	129	104	98	.80	.76
"	9.0	133	95	105	.72	.79
180	9.1	82	69	76	.85	.93
"	22.0	114	91	105	.80	.92

* Concentrations expressed as mg/l or mg/kg of barbital acid.
Values corrected for 90% recovery.

nert(3). For analysis of the compound in brain (cerebral hemispheres) 2 ml of a homogenate containing 0.5 g of tissue were used. The method gave negligible blank values and recoveries averaged 90%. Sodium barbital (100 mg/kg) was given intravenously as a 10% neutral solution to dogs over a period of 5 seconds. After various time intervals, the animals were sacrificed by rapid intravenous injection of 4 to 6 ml of a saturated solution of potassium chloride, which produced cardiac standstill within 5 seconds. Heart blood was immediately obtained by cardiac puncture. Cerebrospinal fluid was withdrawn from the cisterna magna and the brain was then removed for analysis of its barbital content.

Results. Barbital concentrations in the plasma were lower the longer the time interval after drug administration (Table I). Brain/plasma concentration ratios, low at first, reached a maximal value in about 60 minutes. Concentration of barbital in the cerebrospinal fluid rose more slowly than that in the brain (Table I). Cerebrospinal fluid/plasma ratios were low at 3 minutes but became progressively higher reaching unity at 3 hours.

Discussion. Barbital distributes uniformly in total body water; consequently accumulation of the drug in any tissue is limited by amount of water present in that tissue. Since the water content of the brain is about 80% (4) concentration of barbital in brain should eventually be about 80% of that in plasma.†

† Barbital is not appreciably bound to plasma proteins(5).

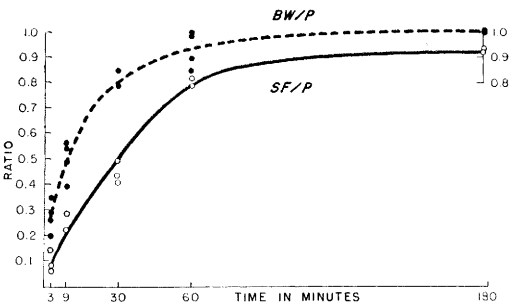

FIG. 1. Brain water/plasma (*BW/P*) and cerebrospinal fluid/plasma (*SF/P*) concentration ratios for barbital given intrav. to dogs. Values obtained from Table I and from previously published(2) experiments, in which only brain water/plasma ratios were determined. Superimposed points are not differentiated.

At equilibrium brain water/plasma concentration ratio should approximate unity. This value was reached in about 60 minutes (Fig. 1). Since cerebrospinal fluid is practically an ultrafiltrate of plasma, at equilibrium the ratio of barbital concentration in cerebrospinal fluid to that in plasma should likewise approximate unity. These results show that there is a barrier to passage of barbital both from blood into brain and from blood into cerebrospinal fluid. The barriers may be similar. The observation that barbital appears in the cerebrospinal fluid even more slowly than in the brain, suggests that the drug may pass from blood into brain and then into cerebrospinal fluid as well as by direct passage from blood into cerebrospinal fluid. The relative contribution of these routes to

entrance of barbital into the cerebrospinal fluid cannot be stated now.

In contrast to the slow passage of barbital into brain and cerebrospinal fluid, the more lipid soluble thiopental passes rapidly into the central nervous system: maximal concentrations appear in the brain almost immediately after intravenous injection(6) and in the cerebrospinal fluid within 7 minutes(7).

Summary. Experiments in dogs have shown that barbital passes slowly into the brain and even more slowly into cerebrospinal fluid. It is possible that the blood cerebrospinal fluid barrier and blood brain barrier are similar for this drug.

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Erythrocyte Extract (Hemolysate) and Tissue Thromboplastin: Their Action on Heparin Activity.* (25611)

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Heparin with its co-factor, which originally was designated albumin X, is a powerful antithrombin(1). By means of certain agents such as protamine(2), toluidine blue(3) and polybrene(4) (a poly 1,5 dimethyl-1,5-diazoundecamethylene methobromide), heparin is inactivated directly and, presumably, stoichiometrically. Tissue thromboplastin also inactivates heparin activity, but from results of earlier studies(5), it was concluded that the anti-heparin action of thromboplastin is indirect, brought about by increase in rate and amount of thrombin produced, thereby exceeding the antithrombin activity of heparin. In the present study an attempt is made to determine the nature of the antiheparin action of erythrocyte extract (hemolysate)(6,7,8). For comparison the antiheparin activity of tissue thromboplastin was restudied.

Materials and methods. Preparation of platelet-poor human native plasma. Blood collected with silicone-coated syringe and needle was transferred to heavy walled test tubes coated with silicone. After chilling in ice bath for 20 minutes, blood was centrifuged for 30 minutes in a Servall Superspeed centrifuge kept in cold room (4-6°C) and the plasma carefully removed with a silicone-coated pipette. *Erythrocyte extract*(9). Human erythrocytes freed from platelets and leucocytes by repeated washing and differential centrifugation were suspended in a volume of physiological saline equal to that of blood from which they were obtained. Complete hemolysis was obtained by freezing at –20°C and then thawing. *Heparin.* One hundred mg sodium salt in 10 ml (Lederle). *Protamine sulfate.* Nutritional Biochemicals Corp. product was dissolved in distilled water. *Prothrombin consumption time with added hemolysate.* In the basic test as previously described(1), 1 ml of native platelet-poor plasma is mixed with a fixed amount of hemolysate and incubated at 37°C. Fifteen minutes after solid clot has formed, it is removed by wrapping it on to a wooden applicator. After 45 minutes of further incubation at 37°C, prothrombin of the serum is determined by the one-stage technic using rabbit plasma adsorbed with $Ca_3(PO_4)_2$ as source of fibrinogen

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