a similar interval. The amounts of the drugs added to the perfusion blood were of the order of 10^{-4} molal. The blood flow was determined at the time the samples were collected by measuring the return flow in a graduated cylinder.

Table I, representing 5 perfusion experiments, shows that following sodium pentobarbital both the glucose and oxygen uptake by the brain was reduced. Following metrazol administration these figures were again increased to about the control levels. It will be noted that the uptake values after metrazol were appreciably greater in 2 of the experiments (3 and 5) than the control values. The probable explanation is that the dogs were given sodium pentobarbital in preparing them for the perfusion and although blood from unnarcotized animals was used for the perfusion, enough narcotic was present in the perfused head to produce some depression at the beginning of the experiment. In some of the experiments, a second injection of the barbiturate was given after the metrazol. The uptake values were again reduced by this procedure. The results of these experiments indicate that barbiturate narcosis inhibits metabolism in the brain, while metrazol has a tendency to reverse this effect.

The corneal reflex served as a guide to the degree of depression in the perfused head. It was present at the beginning of the perfusion, depressed or absent after sodium pentobarbital administration and restored by metrazol.

Summary. The results of perfused head experiments show that during sodium pentobarbital depression there is a measurable reduction in both oxygen and glucose utilization. Metrazol administered during this depression returns the utilization of both to about the control levels or beyond.

13424

A Chemotherapeutic Agent with Osteotropic Properties.

N. ERCOLI. (Introduced by E. Chargaff.)

From the Department of Pharmacology, University of Padua, Italy, and the Pharmacology Laboratory of Hoffmann-La Roche, Inc., Nutley, N.J.

In a search for chemotherapeutic agents with specific osteotropic properties, a study was made of the general mechanism of drug fixation in bone. It has been shown in previous studies[1] that the fol-

[1] Ercoli, N., *Kongressberichte des XVI Internationalen Physiologenkongresses*, Zürich (Switzerland), 1938.

lowing properties are necessary for the fixation of drugs in the inorganic material of bone tissue: 1. Electronegativity of the substance. 2. High degree of diffusibility in the dissolved state. 3. Low solubility of its calcium salt. 4. Formation *in vitro* of an insoluble complex with calcium phosphate. (Properties described under 3 and 4 are interrelated, in that only anions giving slightly soluble calcium salts are adsorbed irreversibly by calcium phosphate.)

For the purposes of this study, a colored bismuth compound (sodium salt of bismuth 1.2-dihydroxy-anthraquinone 3.sulfonic acid) was prepared which meets the above conditions, namely: 1. In this compound Bi is anionic, as demonstrated by electrolysis. 2. The compound is highly diffusible *in vivo* and *in vitro*. In 1.5% agar, the speed of diffusion is 16 mm in 16 hours as compared to that of Congo Red with 10 mm in 16 hours.

In mice, urinary elimination of the bismuth complex occurred 15-20 minutes after i.p. injection of 0.18 mg of bismuth per kg body weight. 3. The calcium salt of the compound has a low solubility. By adding $CaCl_2$ to a solution of the Bi preparation, the calcium salt is precipitated. 4. Ten grams of calcium phosphate adsorb the entire quantity present in 100 cc of a Mol/20 solution of the bismuth preparation. After filtering and washing the calcium phosphate with water, the adsorbed Bi compound can be detected quantitatively.

Sodium bismuth dihydroxy anthraquinone sulfonate, when injected into mice intraperitoneally in doses of 1.5 mg of bismuth per kg of body weight, produces a definite red coloration of bone.

TABLE I.

Drug	Electric charge	Diffusion in agar mm in 16 hr	Solubility Ca salt	Adsorption by Ca phosphate	Fixation in mineral matter of bone	Time required to obtain fixation
Congo Red	—	10	insoluble	++	none	—
Alizarine Red	—	17	"	++	fixed	<30 min
Purpurine	—	16	"	++	"	<30 "
Trypan Blue	—	15	soluble	+	none*	—
Na Bi anthra quinone sulfonate	—	16	insoluble	++	fixed	<30 min
Oxalates	—	>20	"	++	"	not established
Fluorides	—	>20	"	++	"	<35 min[2]
Methylene Blue	+	10		—	none†	—

++ = irreversible; + = reversible; — = non-adsorbed.

* Fixed in the organic matrix of the bone in growing animals. Blotevogel, W., *Zell. and Gewebelehre*, 1924, I/5, 601.

† Fixed in the bone cells in frog. Mitrophanow, P. J., *Biol. Zentralblatt*, 1889, **9**, 541.

[2] Volker, J. F., and Sognnaes, R. F., and Bibby, B. G., *Am. J. Phys.*, 1941, **132**, 707.

This coloration was evident in mice sacrificed 24 and 48 hours after injection, while no coloration of other organs was noticeable. In animals sacrificed 30 minutes after injection, the bone was colored, but dye was found also in blood, liver and spleen.

In Table I, the physico-chemical and osteotropic properties of the above bismuth preparation are compared with that of Alizarine, Purpurine, Congo Red, Trypan Blue, Oxalates, and Fluorides.

From a comparison of the physico-chemical properties of fluoride, oxalate, sulfo-alizarine ions, etc., and the above bismuth compound, it can be assumed that the fixation of the bismuth complex in bone takes place by the same mechanism as reported for these ions, *i. e.*, by the formation of an insoluble complex with calcium phosphate, and simultaneous release of PO_4 ions.[3]

Use of the above bismuth preparation in experimental syphilis in rabbits indicates that it exerts its therapeutic influence after the intravenous injection of 4.5 mg Bi per kg given in 3 divided doses. In mice the tolerated dose by i.v. injection is 2.4 mg Bi per kg compared to 5 mg Bi when given as sodium bismuth tartrate.

13425 P

Electroencephalographic Studies: Slow Activity During Hyperventilation in Relation to Age.

WLADIMIR T. LIBERSON AND HANS STRAUSS. (Introduced by Harry Sobotka.)

From the Neurological Service, Mount Sinai Hospital, New York City.

Previous studies have shown that hyperventilation very easily produces slow activity with frequencies of less than 7 cycles per second (delta activity) in the electroencephalograms of children.[1, 2] However, no systematic research has been undertaken as yet, for studying precisely the relationship between this slow activity and age. Two hundred records taken in the Electroencephalography Laboratory of Mount Sinai Hospital were analyzed for this purpose.

Method. The following groups of patients were examined: (1) idiopathic epilepsy (non-deteriorated), (2) symptomatic epilepsy, excluding patients with brain tumor, (3) non-epileptics with

[3] Ercoli, N., *Boll. Società Italiana Biologia Sperimentale*, 1939, **14**, 16.

[1] Gibbs, F. A., and Gibbs, E. L., *Atlas of Electroencephalography*, 1941, p. 88.

[2] Brill, N. Q., and Seidemann, H., *Arch. Neurol.*, 1941, **46**, 374.