

for a period exceeding two months and had accumulated records of tests on over 200 human patients. Since Eli Lilly and Company was actually preparing pure ergotocin it might justifiably have continued to apply that name to its commercial product. Actually, however, the latter has been given the trade name, "Ergotrate."

The question as to whether or not ergotocin is an "alkaloid" seems to us to be essentially meaningless, since there are no definite chemical criteria by which a substance may be characterized as alkaloidal or non-alkaloidal. In the earlier paper already cited we called attention to the loose usage of the term "alkaloid," and made it clear that our own use of the term "non-alkaloidal" was intended merely as exclusive of the previously known ergot "alkaloids" rather than as chemically descriptive.

It is possible, though not altogether obvious, that the principle responsible for the physiological activity of ergometrine is identical with ergotocin. It is, however, obvious that ergometrine, as described by Dudley and Moir, is not identical with ergotocin. Our own analyses of pure ergotocin and several of its salts indicate the empirical formula  $C_{21}H_{27}N_3O_3$  (C, 68.41 per cent.). (For details, as well as for a discussion of the cleavage products of ergotocin, see the June number of the *Journal of the American Chemical Society*.) Dudley and Moir have announced that ergometrine has a carbon content of 71.46 per cent. The discrepancy would seem great enough to survive any "slight modifications" necessitated by "more drastic purification" of an essentially pure substance. The physiological properties attributed to ergotocin and to ergometrine are similar but evidently differ in degree. The oral dose of ergometrine recommended by Dudley and Moir for human patients is 0.5–1.0 mg; ergotocin is uniformly effective in oral doses of 0.25–0.30 mg. On the whole, the assumption of identity of the active principles appears premature; moreover, that assumption would seem to lead inevitably to the conclusion that ergometrine is impure or partially inactivated ergotocin.

The implication that the chemical investigation of ergot by the present authors was suggested or inspired by Dr. Moir's American addresses seems to us irrelevant to the issue raised. As a matter of strict historical fact, however, our interest in ergot had quite another origin. Neither of us had the pleasure of hearing Dr. Moir during his American visit, nor did we, indeed, hear of him until after we had succeeded in separating ergotocin from the "known ergot alkaloids" late in 1923.

M. S. KHARASCH  
R. R. LEGAULT

THE UNIVERSITY OF CHICAGO

## THIOBARBITURATES

THE report of the hypnotic action of a series of barbituric acid derivatives by Fischer and von Mering<sup>1</sup> in 1903 led to the introduction of barbituric acid compounds into medical practice. Hundreds of substituted barbituric acids and their soluble salts, alone and in various combinations, have been prepared since then in the unceasing search for better products. Some of these compounds have been found to possess valuable therapeutic properties, and their use is rapidly increasing.

Barbiturates may be prepared by condensing urea (or a substituted urea) with derivatives of malonic ester. In a similar way we have prepared a series of thiobarbiturates, using thiourea (or a substituted thiourea), instead of urea. Only a few thiobarbiturates have been previously reported and these have been used merely as intermediates in the preparation of barbituric acid compounds.

There is almost complete lack of pharmacological, clinical and toxicological information in the literature on thiobarbiturates. This may be due to the findings of Fischer and von Mering that the administration of 120 mg per kilo of the sulfur analogue of barbital to a dog produced deep sleep, followed by death. This finding was broadcast by Fraenkel,<sup>2</sup> who deduced therefrom that the presence of sulfur imparts to diethylthiobarbituric acid a pronounced toxic character.

The authors have made and studied a number of thiobarbiturates, finding that they show promise as sedatives. They produce quiet, natural sleep and are free from side actions and from the after-effects observed following the use of their oxygen analogues. This work is being continued and will be reported in detail elsewhere.

ELLIS MILLER  
JAMES C. MUNCH  
FRANK S. CROSSLEY

SHARP AND DOHME  
PHILADELPHIA, PA.

## THE USE OF THE TERM POCONO

IN a recent article George H. Chadwick asks "What is Pocono?"<sup>1</sup> a question which has of late been troubling some stratigraphers in Pennsylvania. From Mr. Chadwick's article it appears that the original definition meant to include certain beds found under-

<sup>1</sup> E. Fischer and J. von Mering, *Therap. d. Gegenw.*, 101: 97, 1903.

<sup>2</sup> S. Fraenkel, "Die Arzneimittel-synthese," 6th ed., 1927, p. 510.

<sup>1</sup> G. H. Chadwick, *Am. Jour. Sci.*, 5th ser., 29: 133–143, 1935.