tified bacteria, including gram positive rods, *E. coli*, streptococci and diplococci, as well as actinomyces, aspergilli and other unidentified molds.

ROBERT GRAHAM
UNIVERSITY OF ILLINOIS

ERGOTOCIN

IT has been found by the authors, working in conjunction with Drs. Davis, Adair and Rogers, of the Department of Obstetrics and Gynecology of the University of Chicago, that the alkaloids ergotoxine, ergotamine, sensibamine are uniformly ineffective when administered orally to human mothers in doses of 2 mg. Larger doses (2–4 mg) often induce unpleasant side reactions such as nausea, vomiting, increase in blood pressure, diarrhea, etc. However, even these large and dangerous doses do not induce contractions in the eighth-day postpartum uterus, in all mothers. While the number of cases studied by us is relatively small (15 cases) these large doses of the alkaloids were found effective only in about 30 per cent. of the cases.

We have found, however, that some fluid extracts of ergot, prepared in accordance with U. S. P. method, were effective in doses corresponding to 3–4 gm of ergot. The activity of these extracts could of course not be due to the known alkaloids (the amounts of these alkaloids as assayed by us were too small to account for the activity), and we undertook the problem of the isolation of the principle responsible for the efficacy of oral ergot dosage. While preparations containing from 60 to 80 per cent. of this principle were obtained by us over a year and one half ago, the isolation of the pure crystalline substance was made only on December 12, 1934. We have called this principle ergotocin. In human mothers this substance is uniformly effective when administered orally in doses of 0.3 mg and intravenously in doses as low as 0.1 mg. The yield of 0.3 mg of ergotocin is roughly equal to from 3 to 4 gms of crude defatted ergot. This principle thus accounts for the activity of the fluid extracts.

Ergotocin has now been used on over 150 patients and no unpleasant symptoms have been observed with it. It controls uterine hemorrhage instantly. Intravenously the effect is noticed within 15 seconds after administration. In the first stages the action of ergotocin resembles that of pituitary extracts, except that its effect lasts for 3 or 4 hours, in marked contrast to the transient effect usually obtained with pituitary extract. In its low toxicity, small dosage, prompt action in uterine hemorrhage, prolonged effect on the uterine muscles, ergotocin is unique among oxytocic principles.

Ergotocin salts, as well as the free base, are white, well-defined crystalline substances. The base melts with decomposition at 155°. The picrate, which is red, melts at from 195 to 197°, with decomposition. The free base is somewhat soluble in water, and the salts are readily soluble. One may obtain even a 10 per cent. aqueous solution of some salts of ergotocin, a unique property among the alkaloids isolated from ergot. Ergotocin differs from the known ergot alkaloids (ergotoxine, ergotamine, sensibamine) in that it is not precipitated by Meyers's reagent in dilutions greater than 1 part in 7,500, while the other alkaloids are precipitated in dilutions of 1: 200,000, to 1: 2,000,000. The optical rotation of the salts of ergotocin so far investigated is positive. The chemistry of ergotocin as well as some of the attempts to synthesize it will be reported as soon as the work now under way is complete.

We believe that with the isolation of this principle ergot therapy can now be put on a rational basis. If one bears in mind that many ergots do not contain this principle (and yet are acceptable on the basis of the U. S. P. assays), the cause of the difference of opinion among obstetricians regarding the value of ergot in obstetrics becomes evident.

The authors wish to take this opportunity to thank most sincerely the Research Corporation, Inc., for a grant which made this work possible and the Eli Lilly Company for generously aiding us in this investigation.

Needless to say, without the cooperation and constant guidance of Drs. Davis, Adair and Rogers, on the clinical and pharmacological evaluation of this principle, this work would not have been brought to a successful conclusion.

M. S. KHARASCH
R. R. LEGAULT
GEORGE HERBERT JONES CHEMICAL LABORATORY
THE UNIVERSITY OF CHICAGO

BOOKS RECEIVED

BROWN, WILLIAM H. *The Plant Kingdom.* Pp. ix + 869. 1040 figures. Ginn. $3.50.

GERLACH, WALTHER and WERNER GERLACH. *Clinical and Pathological Applications of Spectrum Analysis.* Translated from the German by Joyce H. Twyman. Pp. 145. 52 figures. Hilger, London. 15s.

HEISENBERG, WERNER. *Wandlungen in den Grundlagen der Naturwissenschaft.* Nobel Prize Lecture. Pp. 45. S. Hirzel, Leipzig.

KLATZKIN, JAKOB. *Der Erkenntnistrieb als Lebens- und Todesprinzkip.* Pp. 330. Rascher, Leipzig.

LORIA, GINO. *Metodi Matematici.* Pp. xv + 276. 51 figures. Ulrico Hoepli, Milan.

TAMS, W. H. T. *Insects of Samoa.* Part III: *Lepidoptera.* Fasc. 4: *Heterocera.* Pp. 169–290. 12 figures. 13 plates. British Museum, London. 10s.