

on June 12 to the Science Museum, South Kensington, the nacelle of the balloon used by Professors Piccard and Max Cosyns in their second ascent into the stratosphere. Professors Piccard and Cosyns were present and M. Jean Wilhelms, the director of the fund, made the presentation.

TUFTS COLLEGE has completed the construction of a new biological wing of the Barnum Museum. The wing will contain laboratories for histology, embryology, physiology, bacteriology and general biology, as well as offices for the staff. In the entrance hallway has been placed a tablet in memory of Professor Fred Dayton Lambert, who for more than a generation taught biology at Tufts College. The funds for the new wing were left by Phineas T. Barnum.

THE *Philadelphia Inquirer* states that the American Philosophical Society may not accept the bequest of the late William Wood. The residuary estate which the society was to receive was estimated at \$2,000,000 and was to have been used for the erection of a new building. A number of rulings which will affect the amount the society would receive are now under consideration by Judge Charles Klein, of Orphans' Court. Mr. Wood, who was eighty-four and a bachelor, left an estate originally estimated at \$5,000,000. The present accounting shows a balance of \$1,270,571, not including real estate.

A PROGRAM for the expenditure of \$156,298,000 of work-relief funds for forestation in the semi-arid areas of the tree shelter belt zone of the Midwest, as well as in existing foreign preserves, has been advanced by the Forest Service. On May 31 request for the money was made to the Division of Applications in the works program. The forestation program, which would give work in forty-seven states as well as in Alaska, Puerto Rico and the District of Columbia, would be expected to give impetus to the shelter belt project of Dr. Rexford G. Tugwell, Under Secretary of Agriculture. The fund is contemplated for use in a variety of forestry projects. These include such work as the construction and maintenance of fire-

breaks, forest fire lookout houses, towers and observatories, landing fields, telephone lines, forest roads and trails, housing for forest officers, miscellaneous buildings and structures and shelter belt planting.

It is planned to establish, according to the *Journal* of the American Medical Association, in the Rudolf Virchow-Krankenhaus in Berlin a central cancer institute that is to serve all northern Germany. It will be both a therapeutic and a research center. As the first step, a large committee has been appointed, on which, among others, the whole Berlin faculty of medicine will serve, Professor Sauerbruch being the chairman. For this institute, which is to be directed by Professors Cramer and Hintze, a suite of rooms with 300 beds has been selected.

Nature, in reporting the renaming of the Physical Institute of the University of Heidelberg, writes: "The Physical Institute of the University of Heidelberg has recently, in honor of Professor Lenard, been renamed the 'Philipp Lenard-Institut.' A correspondent has sent us a cutting from the students' magazine of that university, giving Professor Lenard's reply to the congratulations of the Heidelberg students on this occasion. The following is a translation of Professor Lenard's reply, and we prefer to make no comment upon it: 'I am very grateful to the students of the University of Heidelberg for their congratulations on the renaming, by the Ministry, of the institute which was built some years ago under my direction. I hope that the institute may stand as a battle flag against the Asiatic Spirit in Science. Our Leader has eliminated this same spirit in politics and national economy—where it is known as Marxism. In natural science, however, with the over-emphasis of Einstein, it still holds sway. We must recognize that it is unworthy of a German—and indeed only harmful to him—to be the intellectual follower of a Jew. Natural science properly so-called is of completely Aryan origin and Germans must to-day also find their own way out into the unknown. Heil, Hitler!'"

DISCUSSION

THE NEW ACTIVE PRINCIPLE OF ERGOT

THE isolation of a new highly important constituent of ergot has recently been announced by Dudley and Moir,¹ and Kharasch and Legault.² Since I³ described

¹ Dudley and Moir, *Brit. Med. Jour.*, March 16, 1935.

² Kharasch and Legault, *SCIENCE*, 81: 388, 1935.

³ Thompson: Doctorate dissertation, Johns Hopkins University, 1934; abstracts published in *Jour. Am. Pharm. Ass'n.*, 21: 853, 1932; 21: 1135, 1932; 22: 736, 1932; 24: 24, 1935; 24: 185, 1935.

the isolation of what is clearly the same substance almost a year before either of these groups of workers, it seems highly desirable that certain facts be presented in order to clarify the rapidly developing confusion and to prevent still more names from being assigned to the same substance.

During the decade preceding 1932, pharmacologists and clinicians accumulated a vast amount of evidence which resulted in what was tantamount to a unanimity

of opinion to the effect that the specific alkaloids ergotoxine and ergotamine were the carriers of the full clinically valuable oxytocic activity of ergot. Consequently, methods of manufacture of and standardization procedures for pharmacopoeial preparations were so selected as to insure the presence of standardized amounts of the specific alkaloidal activity in the finished product,^{4, 5} etc. In June, 1932, Moir⁶ reported the experimental evidence which was responsible for a reopening of the entire ergot problem. Briefly, he clearly demonstrated that the available alkaloids ergotoxine and ergotamine were greatly inferior to crude extracts in their oxytocic activity upon puerperal human patients. Because he obtained prompt and intense activity from aqueous extracts (poor in alkaloids) as well as from hydro-alcoholic extracts (rich in alkaloids), he concluded that the valuable oxytocic activity of ergot resided, not in the specific alkaloids, but in a "new principle as yet unidentified."

Since the publication of a series of ten articles dealing with the pharmacology of ergot in 1929 and 1930, I continued to study the active principles and various extracts on pregnant animals, especially the cat. In August, 1932, approximately two months after Moir's important report appeared, I reported,^{7, 8} similar observations upon the pregnant cat and confirmed his prediction of the existence of a highly important hitherto unidentified principle in ergot by the actual isolation of the substance responsible for the prompt and intense oxytocic activity. The substance had not been obtained in crystalline condition, but was highly active. Contrary to Moir's and Dale's⁹ belief (see also footnotes 10 and 11) this new substance was reported¹² to possess alkaloidal properties. In May, 1934, I reported,^{13, 14} the isolation of the new substance in crystalline form and described its properties, classifying it definitely as a new member of the total specific *alkaloids* of ergot. I did not assign a name to the new alkaloid up to that time because of the almost simultaneous appearance of Küssner's¹⁵

announcement of the new alkaloid "Ergoclovin." To avoid confusion, I called my principle "X-alkaloid" until I was certain of its identity. A comparative study of the properties of the two new alkaloids soon revealed highly significant differences which set them apart as separate entities. Accordingly, also in May, 1934, I assigned the name "Ergostetrine" to my "X-alkaloid."¹⁶ Ergostetrine shows a number of properties which clearly differentiate it from any previously described alkaloid of ergot, but the one difference of greatest possible importance lies in the fact that its oxytocic activity develops much more promptly and much more intensely than even much larger doses of any one or all of the hitherto known alkaloids, including Sensibamine and Ergoclovin.

In February, 1935, there appeared an article by Davis, Adair, Kharasch and Legault,¹⁷ embracing a report presented at the meeting of the Central Association of Obstetricians and Gynecologists, November 1 to 3, 1934, New Orleans, announcing the isolation of the new powerfully and promptly acting principle. In this report, their experimental evidence dealt with a purified amorphous concentrate which was not chemically identified, but which was stated to be *non-alkaloidal* (in agreement with Moir's and Dale's original belief, but in opposition to my identification of the substance). They called this amorphous impure substance "Ergotocin," although they stated in a footnote that they had recently obtained the substance in crystalline form. No evidence as to its identity was given, except that it was non-alkaloidal because it was obtained from their impure non-alkaloidal "Ergotocin."

On March 16, 1935, Dudley and Moir¹⁸ announced that they had isolated the important oxytocic substance in crystalline form. This constituted the first confirmation of my original identification of the new substance as an alkaloid and, it will be noted, it represents a change from the original view held by the British workers (see footnotes 6, 9, 10, 11). This left only the University of Chicago workers¹⁹ opposed to my identification of the new substance as an alkaloid since Dudley and Moir clearly classified their principle as an alkaloid and named it "Ergometrine."

In February, 1935, Koff²⁰ also concluded that the new substance is alkaloidal in nature, although it should be pointed out that his conclusion was based upon the chemical and pharmacological evidence with which I supplied him, his own work consisting wholly

⁴ Fluid Extract of Ergot, U. S. P., 10th revision.

⁵ Liquid Extract of Ergot, B. P., 1932 edition.

⁶ Moir, *Brit. Med. Jour.*, 1119, June 18, 1932.

⁷ Thompson, *loc. cit.*

⁸ Thompson, report presented at the Toronto meeting of the American Pharmaceutical Association, August 22, 1932.

⁹ Dale, Note appended to Moir's report; see footnote 6.

¹⁰ Lecture on ergot by Barger, with discussion, *Pharm. Jour.*, 597, November 18, 1933.

¹¹ Thompson, *Jour. Am. Pharm. Ass'n.*, 24, footnote on page 189, 1935.

¹² Thompson, *loc. cit.*, note 8.

¹³ Thompson, report presented at the Washington meeting of the American Pharmaceutical Association, May 10, 1934.

¹⁴ Thompson, U. S. Patent Office: Application No. 740,199; submitted May, 1934.

¹⁵ Küssner, *E. Merck's Jahresbericht*, 47: 5, 1934.

¹⁶ See footnote 14.

¹⁷ Davis, Adair, Rogers, Kharasch and Legault, *Am. Jour. Obstet. and Gynecol.*, 29: 155, 1935.

¹⁸ *Loc. cit.*

¹⁹ Davis, Adair, Rogers, Kharasch and Legault, *loc. cit.*

²⁰ Koff, *Surg., Gynecol. and Obstet.*, 60: 190, 1935.

of the clinical experiments, which, incidentally, confirmed the validity of my pharmacological approach. Due credit is accorded me in Dr. Koff's report.

In April, 1935, Kharasch and Legault²¹ reported the isolation of their new principle in a crystalline condition, claiming to have obtained it in December, 1934, and naming it "Ergotocin." This is the name originally used for their impure concentrate. It is of interest to note that my Ergostetrine was isolated and identified exclusively in the laboratory, by chemical and pharmacological methods, whereas Dudley's and Moir's Ergometrine and Kharasch's and Legault's Ergotocin were subsequently but independently obtained with the aid of numerous clinical observations upon puerperal humans. The validity of the results obtained by my pharmacological methods was, of course, confirmed by clinical experiments conducted by Dr. Koff and others.

While there is yet much to be done in studying the properties of the new principle, it is believed that the already existing evidence conclusively shows that my Ergostetrine, Dudley's and Moir's Ergometrine and Kharasch's and Legault's Ergotocin are one and the same substance, and that this substance is unquestionably an alkaloid. It is unfortunate that delays in publication have resulted in the confusion already existing. My Ergostetrine was identified as an alkaloid which melts and decomposes at 154 to 155.5 degrees Centigrade, and whose 0.1 per cent. solution in chloroform is laevo-rotatory to the extent of approximately 50 degrees.^{22, 23} Dudley and Moir²⁴ reported their Ergometrine to melt and decompose at 150-152 degrees Centigrade, and the optical activity of a 0.1 per cent. solution in chloroform to be 45 degrees laevo-rotatory. Kharasch and Legault²⁵ state that their Ergotocin (non-alkaloidal?) melts and decomposes at 155 degrees Centigrade, and although they fail to give specific rotation, they state that crystalline Ergotocin "as so far obtained, is dextro-rotatory." In support of my contention that Ergostetrine, Ergometrine and Ergotocin are one and the same substance, it will be noted that my decomposition point is in agreement with that of Kharasch and Legault, but that the optical activity of my Ergostetrine differs from the claim of the same workers. On the other hand, it will be noted that the optical activity of my Ergostetrine is in reasonable agreement with that reported by Dudley and Moir for their Ergometrine, while their decomposition point is definitely lower than for my Ergo-

stetrine. In explanation of these differences, it should be noted that Dudley and Moir admit the possible slight impurity of their crystalline Ergometrine, thus accounting for the slight difference in our respective observations on optical activity and decomposition point. The decomposition point of my crystalline Ergostetrine agrees excellently with that reported by Kharasch and Legault for their Ergotocin. This leaves the only important point of difference among the three named substances to be that Kharasch and Legault report their substance dextro-rotatory, while Dudley and Moir and I agree that the substance is laevo-rotatory. In connection with the latter point which might indicate that the principle isolated by Kharasch and Legault differs from that isolated by myself and that of the British workers, I would point out that through the courtesy of Eli Lilly and Company, I have had the opportunity of examining crystalline Ergotocin. Under identical conditions, crystalline Ergotocin and crystalline Ergostetrine were found to be identical as to decomposition point, optical activity and oxytocic activity on pregnant cats, all data being in agreement with that assigned by me for Ergostetrine.^{26, 27} I consider it a virtual certainty that, as increased amounts of the material become available, others will confirm my contention that the three names have been independently assigned to the same substance.

In April, 1935, I read a paper²⁸ summarizing the pertinent literature and describing the chemical and pharmacologic properties of my alkaloid "Ergostetrine," emphasizing its laevo-rotation (-45 to -50 degrees) in chloroform solution, its decomposition point (154 to 155.5 degrees Centigrade), the fact that it crystallizes readily from chloroform and benzol, less readily from ether, that it gives a strong Cockscorn reaction, and Smith Color reaction, and that it occurs in different lots of ergot to the extent of 0.05 to 0.2 mg per gm. Clinical studies on over 350 puerperal human patients by Dr. Vernon Tuck, of the Philadelphia General Hospital, have been completed and will be reported in due course, the Ergostetrine having been given orally, rectally and intramuscularly. The human dosage is in agreement with that reported by Dudley and Moir and the University of Chicago workers.

Just prior to sending this note to press, a discussion by the British workers in the June 7 issue of SCIENCE came to my attention. With the information at their disposal, I am impressed with their accuracy and fairness, in the treatment of the controversial points. They are laboring under a wrong impression, however,

²¹ *Loc. cit.*

²² See footnote 14.

²³ Thompson, report presented at the Detroit meeting of the American Society for Pharmacology and Experimental Therapeutics, April, 1935.

²⁴ *Loc. cit.*

²⁵ *Loc. cit.*

²⁶ See footnote 14.

²⁷ See footnote 23.

²⁸ *Ibid.*

regarding several phases. Referring to the footnote in my article which appeared in March, 1935, they state that "Thompson reports a later success in crystallizing what was very probably our Ergometrine." That the three independently obtained substances are identical is now established, but I would emphasize that my footnote did not refer to a "later success." This same footnote is contained in the bound copy of my doctorate dissertation, which was accepted by the Johns Hopkins University prior to May 1, 1934, and it constituted a part of my March, 1935, article at the time it was submitted for publication in the *Journal of the American Pharmaceutical Association* on May 10, 1934, more than nine months prior to the announcement of crystalline Ergometrine by Dudley and Moir or the subsequent announcement of crystalline Ergotocin by Kharasch and Legault.

I would add my support to the suggestion by our British colleagues that a single scientific name be decided upon for this new important alkaloid, but unfortunately my name "Ergostetrine" is not a mere matter of "note-book record." This name was both scientifically and legally assigned²⁹ by me in May, 1934. I would emphasize the importance of a universal agreement establishing a single place of registration for new names assigned to complex new plant or animal constituents, without the necessity of patent application to establish a point on a definite date.

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THE CROSS-INOCULATION OF BACTERIAL-PLANT GROUP OF CICER

THE isolation of pure cultures of the root nodule bacteria, cross inoculation and strain efficiency studies on *Cicer arietinum* L. and other species of Indian leguminous crops were conducted by the writer at the University of Wisconsin during 1931-33. It was found that the root nodule bacteria of *Cicer arietinum* L. are specific for that host plant and may be considered a separate group not belonging to the pea group as stated by Simon.¹ A preliminary mention of this finding appeared as a footnote in the monograph of Fred, *et al.*,² and the detailed paper has recently been submitted to the *Indian Journal of Agricultural Science*.

Rasumowskaja³ has recently reported on the specificity of *Cicer arietinum* L. for nodule production and

states that it does not belong to the pea-group. This author does not appear to have noticed the previous mention of this by Fred, *et al.*² His work was confined to inoculation of *Cicer arietinum* with the crushed nodules of *Vicia sativa*, *Vicia cracca* and *Pisum sativum* and pure cultures of nodule bacteria of pea and vetch only, whereas the present writer's conclusions have been based upon studies on cross-inoculations with pure cultures of all the known bacterial-plant groups.

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VITAMINS?

IN the early days of vitamin research, classification by alphabetic order was accepted as a temporary convenience. Indirectly this lettering of unknown, quasi-mysterious substances did much to popularize them and to make the world vitamin-conscious.

The crystallization, the isolation and our more or less definite knowledge of the physiological properties of the so-called vitamins show that there is no longer any scientific basis to maintain such widely different chemical substances as carotenes, ascorbic acid, irradiated sterols, pyrimidine-thiazole compounds, sodium phosphate, manganese compounds, etc., under the same heading, except perhaps for historical purposes.

The academical disagreement between British and American biologists over mere initials to be given to otherwise well-defined products adds to the confusion.

Anti-neuritic, anti-scorbutic, anti-rachitic, anti-anemic, anti-goitric, etc., substances should be classified with the chemical family to which they belong or grouped with the natural or pharmaceutical substances which have closely related physiological properties.

The vague expression "vitamin" will eventually join the musty company of phlogistic, humors, animalcules and kindred antiquated terms.

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CYTOGENETIC NOTES ON SPHAERALCEA AND MALVASTRUM

No chromosome numbers in the genus *Sphaeralcea* have been recorded previously. The only chromosome number reported for a closely related genus is that of 21 pairs in *Malvastrum capense* Gray and Harvey.¹

Recently the chromosome numbers of approximately 15 species, 20 subspecies and 2 botanical forms of the subgenus *Eusphaeralcea* from the southwestern United States have been determined. The basal chromosome number for the subgenus is 5. The prevailing numbers are 5 and 10 pairs, but 15 pairs are of frequent occurrence. Only one form with 25

¹ A. H. S. Stenar, *Akad. Abhand. Upsala*, 1-75, 1925.

²⁹ See footnote 14.

¹ J. Simon, *Centbl. Bakt. (etc.)*, 2 Abt. 41: 470-479, 1914.

² E. B. Fred *et al.*, University of Wisconsin Studies in Science, No. 5, footnote on p. 127, 1932.

³ S. G. Rasumowskaja, *Centbl. Bakt. (etc.)*, 2 Abt. 90: 330-335, 1934.