would, he hoped, "continue to make most effective use of those facilities and funds at our disposal, regarding them as a public trust to be used for the benefit of the public."

Fifteen men, or fourteen per cent. of those employed by the garden, are already serving with the Army and Navy, and more are expected to go. Besides this direct participation in the war, the garden is aiding in many ways in the present emergency. Dr. Robbins then described the new "victory course," in vegetable gardening, one of which is given in cooperation with *The New York Times*. Both afternoon and evening classes are to be given, a three-day short course was offered and a demonstration course in vegetable garden management. The garden will maintain a model vegetable garden out-of-doors during the spring, summer and early fall.

For the relief of present conditions in this country, the garden furnishes information on plants for industries which are suffering the loss of materials through the war.

While the garden has kept strictly within its budget during the past four years, Dr. Robbins pointed out that since its establishment and the construction, around 1900, of the main buildings, no period has witnessed such a marked improvement in material facilities as in the years since 1937. Also, notable horticultural accomplishments can be recorded, and there is evidence on every hand of greater public interest and increased service to the public. He mentioned particularly the following accomplishments:

The number of hardy trees and shrubs in the permanent collections has been doubled.

The number of kinds of plants now cultivated regularly at the Garden is more than 12,000.

The educational program lately initiated and developed attracted more than 400 students last year.

Attendance at the free lectures given on Saturday afternoons has more than doubled (increasing from 3,060 in 1937 to 7,000 in 1941).

Subscriptions to the Garden's monthly journal have grown from 75 to nearly 700 in the past three years.

Most of the conservatory displays have been replanted in naturalistic fashion. Also, the main conservatories were almost entirely rebuilt. (They were first constructed 40 years before.)

The Garden's 280 acres were completely surrounded by a fence for the first time.

Much reconstruction was done in the Museum Building, including installation of a reception room for members.

Considerable new construction was added to improve the facilities for growing plants.

Arrangements for a new base plan for the future development of the garden have been completed. Major Gilmore Clarke is now working on the plan, which has been made possible through the generosity of Mrs. Harold I. Pratt, a member of the Board of Managers. The fencing of the grounds in 1940 has made necessary a number of changes in landscaping and in traffic routing.

Accomplishments of the year 1941 include:

Beginning of construction of a walled experimental garden for the use of members of the scientific staff.

Receipt of many thousands of plants as gifts, a number of them extremely rare, and among them the Forster collection of nearly 10,000 orchids valued at $75,000; 2,000 cactus plants from the Government of Mexico; and a total of 4,000 bulbs, orchids and other plants from two individual donors.

Nearly 50,000 individual plants set out (chiefly in front of the Main Conservatories and the Museum Building) for bedding effects in the spring and summer. These included 10,000 tulips saved from the display of the previous year, which had been a gift of the Holland Bulb Industries.

More than 4,000 shrubs planted on the grounds, including large numbers of rhododendrons, flowering cherries, barberries, lilacs, evergreens and other ornamentals. New labels required for these and other plants in cultivation at the Botanical Garden during the year totaled more than 5,400. Of these 49 were of the informational type, placed mostly beside plants of economic usefulness.

Addition of 36,747 herbarium specimens to the scientific collections, bringing the total of this important reference collection of preserved plants to 2,056,296 specimens, comprising the largest herbarium under one management in the United States.

Addition of books to bring the total bound volumes in the library close to the 50,000 mark.

Officers of the garden, all reelected for the current year, are: Joseph R. Swan, *President;* Henry De Forest Baldwin and John L. Merrill, *Vice-presidents;* Arthur M. Anderson, *Treasurer;* and Henry de la Montagne, *Secretary.*

SPECIAL ARTICLES

NARCOTIC POTENCY OF BIURETS CONTAINING PIPERIDINE

HILL and Degnan[1] noted that 1-diethylacetyle-5,5-cyclopentamethylene biuret has hypnotic properties and comparatively low toxicity. Following a different chemical procedure than previously employed, 4 additional biurets have been synthesized.[2] These are:

[1] A. J. Hill and W. M. Degnan, *Jour. Amer. Chem. Soc.*, 62: 1595, 1940.

[2] C. H. Ch'eng and Peter P. T. Sah, in preparation.

1-diphenyl-5-phenyl biuret (m. p. 134° C.), 1-phenyl-5,5-pentamethylene biuret (m. p. 153° C.), 1,1-pentamethylene-5,5-pentamethylene biuret (m. p. 198° C.), and 5,5-pentamethylene biuret (m. p. 121° C.).[3] All derivatives are crystals and the first 3 are poorly soluble in water or alcohol. One per cent. water solution of 1,1-pentamethylene-5,5-pentamethylene biuret may be made by heating and keeping the solution at 37° C.

The monopiperidine biuret is less toxic for mice than sodium barbital, sodium pentobarbital or sodium dilantin but more toxic than paraldehyde. The LD_{50} for mice is 600 mg/kg on intraperitoneal injection. This amount antagonizes a surely fatal dose of picrotoxin and usually of strychnine but does not protect mice against cocaine.[4] Hypnotic doses of the biuret in rabbits of 60 mg/kg given intravenously slightly depress blood pressure and cardiac rate during the injection only, but do not affect respiration or uterine activity.[5] Inhibition of uterine strips, from humans and rabbits occurs in dilutions of 1:2,500 to 1:5,000 *in vitro*. It is 30 and 10 times less potent than sodium dilantin and sodium pentobarbital, respectively. The total oxygen uptake of rat liver during a 60-minute period is depressed approximately 35 per cent. by the monopiperidine biuret, 0.1 gm/100 cc; 75 per cent. by sodium pentobarbital, and inappreciably by paraldehyde and sodium barbital.[6]

Dipiperidine biuret is even less toxic for mice, the LD_{50} being 1,250 mg/kg on intraperitoneal injection. It is less active as an antagonist of chemicals affecting different levels of the central nervous system. It antagonizes cocaine convulsions but does not save mice given lethal amounts; no protection against strychnine convulsions is provided, and all picrotoxin-treated mice had convulsions after an LD_{50} dose of this biuret but none died. In rabbits, narcosis follows intravenous injections of from 100 to 200 mg/kg without appreciable effect on respiration, on blood pressure except during the injection, or on the blood sugar during or following narcosis. Uterine activity *in situ* is inhibited with these doses. *In vitro* tests indicate that smaller concentrations of the dipiperidine than of the monopiperidine biuret are inhibitory. Dilutions of 1:7,500 to 1:10,000 for human uterine strips and from 1:15,000 to 1:20,000 for rabbit strips are effective. In this respect the dipiperidine biuret resembles sodium pentobarbital. Depression of oxygen consumption of rat liver follows exposure to 0.1 gm/100 cc of this agent for 60 minutes.

Since the dipiperidine derivative has pharmacologic activities similar to sodium pentobarbital, except that it is 1/10 as toxic, the narcotic potency at various dose levels was studied in inbred white mice and inbred white rats. The graph indicates the duration of narcosis in mice after intraperitoneal injection in single or divided amounts. Preliminary studies after oral administration to rats provided similar data. At the onset of narcosis there is no excitement and during the depth of narcosis respiration is more regular and less depressed than noted in pentobarbital treated animals.

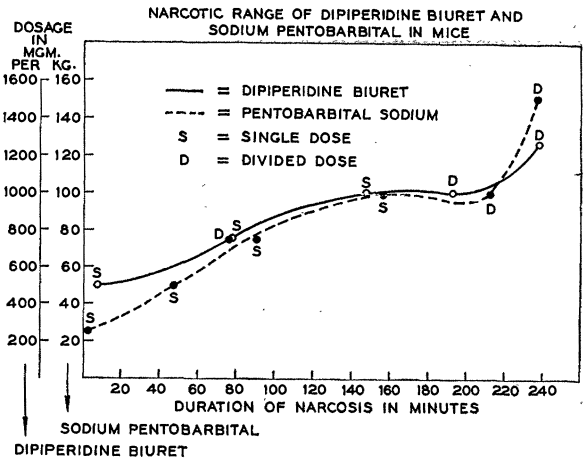

FIG. 1.

Preliminary observations on the effect of the dipiperidine biuret in 60 and 120 mg/kg doses intravenously in the rabbit at term indicate that fetal respiratory movements are not significantly affected by these amounts.[7]

Summary: Five biurets, 4 containing piperidine, have been prepared and various pharmacologic activities of 2 have been studied. The monopiperidine derivative effectively antidotes picrotoxin and strychnine, while the dipiperidine biuret is life-saving to mice given lethal doses of picrotoxin. Uterine activity and the oxygen consumption of rat liver are depressed more by the dipiperidine biuret. Neither derivative appears to be as toxic as commonly used hypnotics or anticonvulsants with which a comparison was made, except paraldehyde. Narcosis of mice,

[3] We are grateful to Dr. Stanley Wilson, Yenching University, for checking nitrogen determinations of these compounds.

[4] C. H. Ch'eng, H. H. Anderson and S. Y. P'an *Jour. Pharmacol. and Exper. Therap.*, 72: 7, 1941; H. H. Anderson and S. Y. P'an, *Proc. Soc. Exp. Biol. and Med.*, 46: 611, 1941.

[5] S. Y. P'an and C. S. Lu, *Chin. Jour. Physiol.*, 16: 311, 1941.

[6] S. Y. P'an and C. S. Lu, in press.

[7] K. T. Lim, personal communication.

rats and rabbits produced by the dipiperidine biuret resembles that of pentobarbital but is less disturbed.

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FLUORINE ACQUIRED BY MATURE DOG'S TEETH[1]

THE post-eruptive deposition of fluorine in the enamel[2,3,4] and dentine[3,4] of molar teeth of young rats has been reported. A similar study on a mature dog supports this finding particularly with regard to the dentine. At the beginning of this study a two-year-old mongrel dog with full dentition had three representative teeth extracted. Sodium fluoride was then given via food and drinking water for definite periods, each period terminating with the extraction of two or three comparable teeth. Food and drinking water were consumed ad libitum. The pooled teeth representing each period of exposure to fluoride were separated into dentine and enamel and analyzed for ash and fluorine.

TABLE I

EFFECT OF EXPOSURE TO FLUORIDE ON THE FLUORINE CONTENT OF THE DENTINE AND ENAMEL OF A MATURE DOG'S TEETH

		I	II	III	IV	V
Pooled teeth sample number						
Age of dog at time teeth were extracted.	(days)	730	796	900	1,145	1,289
Total number of days exposed to fluoride in food and water prior to tooth extraction	(days)	0	66	170	415	559
Exposure to fluoride immediately prior to tooth extraction.						
Fluoride in food and water	(ppm)	0	15	45	100	500
Total time fed	(days)	0	66	104	245	144
Composition of dentine						
Ash	(per cent.)	71.90	71.88	73.15	73.35	73.21
Fluorine	(per cent.)	.018	.022	.039	.059	.072
Composition of enamel						
Ash	(per cent.)	95.20	95.75	95.72	96.32	95.96
Fluorine	(per cent.)	.006	.007	.009	.007	.011

The results for each successive sample of dentine show that the mature dentine increased in fluorine decisively. The enamel does not show a similarly consistent nor equal percentage-increase. The final sample of enamel, however, contained 0.011 per cent. fluorine as compared with 0.006 per cent. fluorine in the initial or control enamel. In this connection it is interesting to note that the enamel of carious human teeth and the enamel of non-carious human teeth have been reported to contain 0.0069 per cent. and 0.0111 per cent. fluorine, respectively.[5] A distinction possibly may be made in tooth fluoride acquired post-eruptively and fluoride which is acquired during the formative period of the tooth.[3,4] Fluoride given during gestation and lactation to mother rats, *i.e.*, during the period of tooth formation in their young, appears to diminish susceptibility to caries in the offspring.[6] There is certain limited epidemiological evidence with respect to human dental caries,[7] which seems to agree with this latter finding in rats.[6]

These results for the dog's teeth and similar results based on young rats[2,3,4] advance speculation regarding post-eruptive chemical modification, as a property of calcified dentine and enamel. Fluoride retention may prove a useful tool in studying individual variations in dentine and enamel in relation to tooth age and susceptibility to dental caries. In the results for the enamel fluoride the property of the enamel to adsorb fluoride on the oral surface[2] may receive further support, although a systemic retention via the dentine can not be discounted.[3,4]

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FURTHER NOTES ON THE INCUBATION PERIOD OF THE PEACH MOSAIC VIRUS[1]

ADDITIONAL information regarding the seasonal spread of peach mosaic from diseased to healthy trees and the incubation period of the causal virus has been obtained during the 1941 growing season.

Seeds from "natural" peach seedlings are used in

[1] The author is indebted to Passed Assistant Dental Surgeon Francis A. Arnold, Jr., for assistance in the experimental work.

[2] M. W. Perry and W. D. Armstrong, *Jour. Nutrition*, 21: 35, 1941.

[3] F. J. McClure, *Jour. Nutrition*, 22: 391, 1941.

[4] F. A. Arnold, Jr., and F. J. McClure, *Jour. Dent. Rsh.*, 20: page 457, 1941.

[5] W. D. Armstrong and P. J. Brekhus, *Jour. Dent. Rsh.*, 17: 393, 1938.

[6] G. J. Cox, M. C. Matuschak, S. F. Dixon, M. L. Dodds and W. E. Walker, *Jour. Dent. Rsh.*, 18: 481, 1939

[7] H. T. Dean, P. Jay, F. A. Arnold, Jr., and E. Elvove, *Pub. Health Rep.*, 56: 365, 1941.

[1] Published with the approval of the director as paper number 130, Scientific Journal Series, Colorado Agricultural Experiment Station.