

perience in one or more of the following: Paid experience in technical radio work such as radio repairman, operator or electrician; technical study in residence at a radio school; resident study including courses in radio in a school of engineering or technology; completion of an approved defense training course in any branch of radio work. An announcement by the commission states that the constantly increasing activities of the Navy Department call for many inspectors of aeronautical engineering materials. For many months the commission has had open an examination for inspectors covering several branches of aeronautical engineering materials. Provisions for using national defense training courses to meet the experience requirements have been liberalized. The positions pay from \$1,620 to \$2,600 a year, and the maximum age is 65 years.

THE New York Academy of Medicine announces the availability of the Louis Livingston Seamon Fund for the furtherance of research in bacteriology and sanitary science. Two thousand dollars is available for assignment in 1941. The fund will be expended only in grants in aid for investigation or for scholarships for research in bacteriology or sanitary science. Grants may be used for technical help, for aid in publishing original work or for the purchase of necessary books or apparatus. The fund is administered by a Committee of the academy under the following conditions and regulations: Communications should be received before November 1 by Dr. Wilson G. Smillie, chairman of the Louis Livingston Seaman Fund, 1300 York Avenue, New York City.

THE Louise A. Boyd Arctic Expedition of the National Bureau of Standards, which sailed from Washington on June 11, is expected to return about November 1. Both Miss Boyd and Captain Bob Bartlett, who commands the expedition schooner *Effie M. Morrissey*, are Arctic explorers of wide experience. They planned to observe the ionosphere characteristics as

determined by special radio measurements, geomagnetism, auroral manifestations and also to measure ultraviolet light intensities. The expedition, under the leadership of Dr. Louise A. Boyd, was undertaken at the request of the Government, Dr. Boyd having been appointed a consulting expert of the National Bureau of Standards. The U. S. Coast Guard and the Department of Terrestrial Magnetism of the Carnegie Institution cooperated in the arrangements for the expedition.

At a dinner of the citizens of Chicago on September 26 at which the attendance was 800, it was reported that \$9,200,000 had been subscribed to the fiftieth anniversary fund of \$12,000,000 of the University of Chicago. It is planned to raise the balance of the money over a period of five years.

THE Congress of the United States on September 15, as reported in the *Journal* of the American Medical Association, completed legislative action on a bill authorizing the War Department to purchase for \$1,000,000 a site near the Folger Shakespearean Library for the new Army Medical Library and Museum to cost \$3,750,000.

THE School of Medicine and Dentistry of the University of Rochester received more than \$900,000 last year through the will of Dr. Henry C. Buswell. It will now receive the same amount under the will of his wife, Mrs. Bertha H. Buswell. Mrs. Buswell died on July 30. Her will makes available ultimately to the Medical School a trust fund of \$925,164.

A LARGE collection of cactus plants, a gift of Mexico to the United States, was taken to the New York Botanical Garden on September 1 after a two months' display at Rockefeller Center, to be made a permanent part of the cactus collection. The gift was officially accepted last July by Dr. William J. Robbins, director of the garden.

## DISCUSSION

### THE EFFECTIVENESS OF EQUIMOLAR QUANTITIES OF VARIOUS CARDIAC GLYCOSIDES

It has recently been re-emphasized<sup>1</sup> that the human therapeutic doses of the several pure cardiac glycosides are not predictable from animal toxicity assays. It has, apparently, not been pointed out that in the cases of certain comparable glycosides for which the single dose, or short-time interval multiple intravenous dose, for "full digitalization" in auricular fibrillation is known, there is remarkably small difference in the

molar quantities of the drugs necessary to produce comparable effects. Furthermore, in at least one glycoside differing from others in the chemical configuration at the C<sub>3</sub> position the molar quantities of drug necessary to produce comparable therapeutic effects are widely different.

In the accompanying Table I are shown the intravenous "full digitalizing doses" for auricular fibrillation, together with cat lethal assay figures and certain chemical data for five pure glycosides and one mixture. It will be noted that, for the first four sub-

<sup>1</sup> H. Gold and McK. Cattell, *SCIENCE*, 93: 197, 1941.

stances listed, the full therapeutic doses expressed in micromols are of similar magnitude. The agreement is better than that obtained if animal lethal potencies are compared. In these four glycosides the hydroxyl

TABLE I

Glycoside	Molecular weight	Intra-venous digitalizing dose for man		Cat lethal micromols*	Configuration C <sub>3</sub>	Sugar
		mg	micromols†			
Ouabain	584	1.0 <sup>2</sup>	1.7	0.21	$\alpha$ -OH	Rhamnose
Digitoxin	764	1.2 <sup>3</sup>	1.6	0.43	$\alpha$ -OH	Digitoxose
Lanatoside C	984	1.5 <sup>4</sup>	1.5	0.22	$\alpha$ -OH	Digitoxose
Digoxin	780	1.0 <sup>5</sup>	1.3	0.28	$\alpha$ -OH	Digitoxose
		1.5 <sup>6</sup>	1.9			
Thevetin	858	4.2 <sup>7</sup>	4.9	1.06	$\beta$ -OH	Digitalose?
Scillaren A and B	692	0.5 <sup>8</sup>	0.7	0.22	no-OH?	Rhamnose
		0.7	1.0			

\* The correction for water of crystallization has been neglected in these calculations. The value is unknown for the materials used by the several investigators. If the proper correction could be applied the molar dosages would be smaller, the largest correction probably being for ouabain.

at C<sub>3</sub> in the nucleus has the  $\alpha$  configuration. Fieser<sup>9</sup> has pointed out certain correlations between physiological activity measured by toxicity and the configuration at the C<sub>3</sub> position.

In the case of thevetin the human intravenous dose in question is about three times as great as in the first four on a molar basis. In this glycoside the hydroxyl at C<sub>3</sub> has the  $\beta$  position.

On the basis of one report on the use of a mixture of Scillarens A and B a somewhat lower effective dose is indicated. The structures of Scillarens A and B have not been satisfactorily investigated, but absence of the hydroxyl at C<sub>3</sub> has been reported.

The comparable full therapeutic doses for the glycosides ouabain, digitoxin, lanatoside C and thevetin are satisfactorily established. In the cases of the other glycosides less extensive studies have been made. Moreover, it must be pointed out that the criterion of effectiveness in studies on rapid digitalization in auricular fibrillation is an arbitrary one, namely, a reduction in pulse rate, usually to 80 per minute or below, within a specified time. Although it has fre-

<sup>2</sup> J. Wyckoff and W. Goldring, *Arch. Int. Med.*, 39: 466, 1927.

<sup>3</sup> H. Gold, N. Kwit and McK. Cattell, *Jour. Pharmacol. and Therap.*, 69: 177, 1940.

<sup>4</sup> N. Kwit, H. Gold and McK. Cattell, *Jour. Pharmacol. and Therap.*, 70: 254, 1940.

<sup>5</sup> Medical Research Council of the British Medical Association.

<sup>6</sup> E. Schwab, *Texas State Jour. Med.*, 35: 619, 1940.

<sup>7</sup> H. Arnold, W. Middleton and K. Chen, *Am. Jour. Med. Sci.*, 189: 193, 1935.

<sup>8</sup> L. Zwillinger, Wien, *Arch. f. inn. Med.*, 31: 201, 1937.

<sup>9</sup> L. F. Fieser, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold, New York, 1937.

quently been so assumed, there is no satisfactory proof that this initial slowing of the pulse is due entirely or majorly to an effect upon the heart directly. In fact, since it is largely abolished by atropin, the early slowing is probably not due to a primary action on the heart, but rather to one upon the nervous cardio-regulatory mechanism. Cushny<sup>10</sup> showed that the early rate changes in digitalization in auricular fibrillation are mediated by vagal influences.

It is by no means certain that the approximate identity of molar doses for full digitalization in fibrillation reported for the first four glycosides in Table I would be found if other criteria were employed. The lack of corresponding agreement in cat lethal doses points to such differences in regard to certain actions at least.

It may be noted that there is no apparent correlation between the nature of the sugar in the glycoside and the physiological action in question.

Attention is being called to the remarkable coincidence of human intravenous doses of several pure glycosides for a particular effect, not so much because it is believed that the configurational peculiarity referred to is more important than others may be found to be, particularly if other criteria of effectiveness are studied, but rather to emphasize the possibility and desirability of further studies in the direction of correlation of action with structure.

MAURICE B. VISSCHER

JOHN S. LADUE

UNIVERSITY OF MINNESOTA

#### A NOTE ON SZENT-GYÖRGYI'S "TOWARD A NEW BIOCHEMISTRY"

IN his recent paper<sup>1</sup> Professor Szent-Györgyi advances the hypothesis that a quantum of energy, made available at one point in a living system by chemical action or absorption of light, for example, may be transmitted to a relatively distant point of the system without degradation or dispersion, there to cause some highly localized reaction, such as photosynthesis or the splitting of a protein. The examples cited by Professor Szent-Györgyi prove, of themselves, that this brilliant hypothesis must be considered in any future biochemical or biophysical speculation.

Professor Szent-Györgyi postulates, in his paper, that the mechanism whereby this energy is transmitted is that which has proved effective in fluorescent crystals of ZnS and other substances, the excitation of an electron to an unfilled extended state "belonging" to the entire structure rather than to one or two atoms. To the present writers, this second postulate would appear to limit seriously the generality of the original

<sup>10</sup> A. Cushny, "The Action and Uses of Digitalis and Its Allies," Longmans, Green and Co., London, 1925.

<sup>1</sup> SCIENCE, 93: 609, 1941.