Comments and Communications

The Structure and Activity Relationships of the Choline Group of Drugs Determined by Measurements of Phase-Boundary Potential

The interesting paper of Ing (*Science*, 1949, **109**, 264) presents data exposing discrepancies in the proposal made by Pfeiffer that muscarinic action is produced by a spatial molecular configuration (*Science*, 1948, **107**, 94). Both authors have pointed out pharmacologically important features of the structural formulas of cholinergic substances but no mention is made of the lipoid solubility or electrogenic properties of the compounds described.

Twenty years ago, the senior author (Beutner, R., *J. Pharm. exp. Therap.*, 1927, **31**, 305) reported the outstanding phase-boundary potential of alkaloids and recently the transient potentials (waves) of acetylcholine were described (Seventeenth International Congress of Physiology, Abstracts of Communications, p. 390, 1947; Second International Congress of Electroencephalography, Paris, 1949). These investigations of the essential or electrical action of cholinergic drugs show that pharmacodynamics must deal with energy relationships and attempt to discover the mechanism underlying the relation of structure to action. We have measured the phase-boundary potentials of choline and acetylcholine and also determined the ohmic resistance of the oils shaken with choline and acetylcholine. Acetylcholine chloride, at a concentration of 0.0027 M, produced 35 mv negativity at the interface between saline and guaiacol, reducing the resistance from 2.4×10^6 to 2.7×10^5 ohms. In the same apparatus, 0.0027 M choline chloride produced only 5 mv negativity, and reduced the resistance of the oil from 2.4×10^6 to 8.0×10^5 ohms.

These data throw light on the mechanism of action of this type of drug. Acetylcholine is a stronger cholinergic drug because it penetrates into the lipoid, and because after penetration it ionizes in the nonaqueous phase. For these reasons there is a higher ion concentration in the lipoid at the site of contact with acetylcholine. This in turn entails a larger negative potential at the lipoid surface. Such a variation is the essential factor in nerve activity. Changes in these physical properties are produced by the introduction of acetyl groups in choline, as our data show. Ing assigns special significance to the size of the "cationic head" of a cholinergic drug and to the charge on the N- atom. Without doubting the justification for these assumptions, we believe that these are factors influencing ionization in the lipoid phase and consequently of secondary importance for the pharmacological effect. The influence of the exchange of ethyl for methyl groups in acetylcholine would likewise exert pharmacological effect primarily through influence on the electrogenic properties of acetylcholine, and this holds also for other substitutions.

We agree with Ing that the term *prosthetic* applies to the acetyl group. In conclusion, it would appear that the "cationic head" of Ing, the "prosthetic groups" of Pfeiffer, and the "positive charge on the central nitrogen" of Taylor (*Nature*, 1947, 159, 86) are nothing more than ionization factors in the phase-boundary potentials of alkaloids previously described (cf. Beutner 1927).

T. Cunliffe Barnes and R. Beutner
Department of Pharmacology,
Hahnemann Medical College and Hospital, Philadelphia

Geological Applications of Short Range, Two-Way Radio Sets

Recent success with portable, short range, two-way radio sets ("walkie-talkie") in instruction of students in field geology suggests many possible applications of this or similar devices in educational and professional work.

The short range two-way radio, designed for voice conversation, is described in the War Department's Technical Manual No. 11-235, May 14, 1943, pp. 2–4 as a press-to-talk, portable, radio telephone, receiving and transmitting on the same frequency. The total weight of the set, including batteries, is 5.5 lb. The radio receiver is battery-powered; batteries should last about 15 hr under almost continuous operation.

Graduate field courses in geology, conducted as a part of the regular curriculum of class work at Louisiana State University, have for some time posed a problem in how to instruct these students properly in the field. These classes, in many instances, travel long distances between individual outcrops or type areas. Geologic and geomorphic features of considerable importance in student training often are present between such localities. In order to provide properly trained personnel for each car participating in these class trips, the enrollment previously has been restricted to a number sufficient to fill two cars. The increased graduate enrollment of the last few years, and the consequent increased demand for this type of course, has resulted in classes too large for proper instruction.

Recently, the technique of equipping each car with a portable, short range, two-way radio set was tried. Six cars and 24 students participated. One staff member, acting as trip leader, rode in the lead car; by means of the radio telephone he gave directions and instructions, and kept up intermittent discussions of various features encountered between the individual stops.

Signals for communication between cars were given by white flags or horns. In areas of sufficient interest, sets were kept on constantly; otherwise they were shut off until flags signaling communication were flown.

To overcome shielding and absorbing of signals by the metals in the car, aerials were extended outside the cars at all times during communication. For similar reasons, it was necessary to prevent contact of the aerial with the metals of the car.

The considerable success attained with this technique in so large a group allows for similar and related uses in field parties of various kinds. Such applications can be applied easily to almost any type of field investigation or construction operation utilizing more than one man.

GROVER E. MURRAY

Louisiana State University, Baton Rouge

Longevity of the Tropical American Toad, *Bufo marinus* L.

Though toads are known to live for many years, there are few published records detailing the methods under which longevity tests have been conducted. In the experiment described here the toads were confined in a cage 8 ft long, 4 ft wide, and 2 ft high. It was covered with strong, galvanized screen of 1/8-in. mesh, attached to a heavy framework of concrete posts. Iron sheeting, 1 ft wide, was imbedded vertically in the ground just inside the walls to a depth of 6 in. This was to prevent any possibility of toads' burrowing out. A strong door, provided with a padlock, was built in the top of the cage.

To get toads for the test, eggs were collected on May 26, 1933, from a reservoir near Honolulu, where a female *Bufo*, attended by a male, had been observed laying an egg string. Some of the eggs were placed in a pan of water and hatched on May 29. The larvae were given green algae and boiled rice, on which they thrived. Metamorphosis was completed by June 30 and the toadlets, measuring about 6 mm in length, were placed in the cage. The ground was kept wet, and the cage was partially shaded. A small brick-lined retreat was constructed in one corner. Quantities of ants were supplied for food at frequent intervals. Within a few weeks the toads had grown sufficiently to take larger insects, and by October 1, when they were 3 months old, they were from $2\frac{1}{2}$ to 3 in. long and able to swallow almost any insect given them.

The experiment started with 26 toads. By the time they were 6 months old, when many of them had reached a length of 4 in., the problem of feeding them sufficient insects became acute. The population was thinned to nine toads, consisting of five females and four males. By setting appropriate traps, cockroaches were caught to feed the toads. Many hundreds of roaches were placed in the cage weekly. A large pan of water was also supplied, but none of the confined toads ever laid any eggs.

This experiment continued until May 14, 1949, when the last toad—a large female—died, after being under almost daily observation for 15 years, 10 months, and 13 days. She had consumed during her lifetime, according to our estimate, about 72,000 cockroaches. The other eight toads in the test had lived from $8\frac{1}{2}$ to 14 years.

C. E. PEMBERTON

Experiment Station, Hawaiian Sugar Planters' Association, Honolulu

Some Problems in Sensory Prosynthesis

There is at present a very considerable amount of interest in devices by which lost senses can be replaced or at least compensated for. At the Massachusetts Institute of Technology the authors have been working on a method of replacing hearing by tactile stimulation. In this method a sound is carried from a microphone to a bank of filters. The output of each of these filters, except possibly the low frequency stage, is rectified and used to modulate a low frequency carrier and the output of these carriers as well as of the possibly by-passed low frequency stage, is carried to a number of stimulators, which may be properly designed electrodes or may be electromagnetic vibrators resting on suitable points of the skin, such as the five fingers. This produces a pattern of stimulation which we have already proved by experimentation to possess a high degree of recognizability and which we hope ultimately to embody in a portable apparatus by which we expect that the totally deaf can participate in active speech.

In designing this apparatus we have first had to convince ourselves by the theory of the Vocoder that the amount of information which could be transmitted by this transmitter, on the basis of acoustical speech, was of sufficient magnitude to furnish an adequate basis for the understanding of words. We then worked on the principle that in using an inferior sense, such as touch, it was necessary to cut the incoming information to that which is semantically sufficient so as not to overload the receptors of the skin and prolong the learning period. In doing this we have had to transfer part of the cortical function of the ordinary hearing mechanism to an electrical system outside the body. The severe limitation of the amount of information which exists when one tries to transfer one of the cortical functions to an external machine should be a guiding principle in other sensory replacements, such as those for the blind.

It is most important in all such prosthetic apparatus that the patient should not separate the problem of active communication, such as speech, from that of passive communication, such as hearing. In the normal individual, speech is maintained at a high level only by the continual monitoring of the speaking person in which, at no time, is he unable to compare his own speech with that of others. This is equally important, or even more important, in artificial methods of communication such as we are devising. The portability of the apparatus is not an advantage, but it is a necessity.[1] Under these conditions, as we have already demonstrated experimentally, the patient immediately begins to improve the quality of his speech by comparison and his voice begins to lose its deaf-mute deadness.

We suggest these principles as a basis for further work in sensory replacement.

J. WIESNER, N. WIENER, and L. LEVINE

*Research Laboratory of Electronics
Massachusetts Institute of Technology, Cambridge*

[1] The importance of feedback in the learning process is discussed at length in the book *Cybernetics* by Norbert Wiener, published by John Wiley & Sons. The apparatus employed in the course of the research reported above is described in the December 15, 1948 *Quarterly Progress Report* of the Research Laboratory of Electronics, Massachusetts Institute of Technology.