But working with excised vagus nerves and ganglia, Lissák[13,14] reports a regular release of A.Ch. Apparently, excision creates a greater degree of departure from normal conditions than does perfusion. Be that as it may, Lissák's results lend strong support to my conclusion that the A.Ch. metabolism is a process that is not specific to synaptic junctions.

The results obtained by Lissák may have invalidated my conclusion that entrance into the ganglion cells of impulses conducted in the antidromic direction may result in the release of A.Ch., if the proper conditions for the release have been created. When the postganglionic trunk is stimulated, the escape of the stimulus to the preganglionic trunk is easily prevented, but not escape to the neighboring nerve trunks. Consequently, as the stumps of the X and XII nerves are included in the perfused mass of tissue, the possibility exists that the "antidromic" A.Ch. actually was released by the cut ends of these nerves. This explanation would undoubtedly be adequate, but it would become necessary only if the existence of A.Ch. in ganglion cells should be disproved. Brown and Feldberg[15] report that ganglion cells contain some A.Ch. This statement is denied by Lissák,[16] although Loewi and Hellauer[17] found some A.Ch. in the postganglionic trunk.

Whether the A.Ch. that may be released by preganglionic stimulation is released only, or at least chiefly, at the synapses, has not been demonstrated up to the present time. Direct proof of the synaptic origin was believed to have been obtained in blocking experiments.[18] However, a fundamental, but apparently little known observation of de Castro[19] has demonstrated that nicotine does not paralyze the ganglion cells, but does act on the presynaptic fibers. Therefore, the release of A.Ch. during the nicotine block proves that at least a part of the A.Ch. is released by the presynaptic fibers, and consequently no proof exists that synapses are a more generous source of A.Ch. than the rest of the presynaptic fiber.

Another point under discussion is whether the release of A.Ch., when it does take place, follows the temporal course of synaptic transmission. When using the original technique for the perfusion of the ganglion,[20,21] in several experiments I found, in agreement with Feldberg and Vartiainen, that A.Ch. was released or its output increased only during the periods of stimulation of the preganglionic trunk. But later with the use of the new technique I found, this time in agreement with observations made by Barsoum, Gaddum and Khayyal,[22] that the output of A.Ch. may considerably outlast stimulation and synaptic transmission. MacIntosh did not observe delayed outputs of A.Ch. and interprets the delayed output in my experiments as a delayed removal of A.Ch. that had been released during stimulation. Without further experimental evidence this question can not be definitively settled; nevertheless, it must be remarked that if the delayed outputs of A.Ch. should have been due to delayed removal, then no significant immediate outputs would have been observed in my experiments, while in fact immediate and delayed outputs were repeatedly observed in the same experiment, the immediate outputs often being the larger.

In conclusion, the fundamental observation of Feldberg and Vartiainen, which has been considered as the direct proof of the chemical theory of synaptic transmission,[23] included several essential points: A.Ch. is released in given amounts at the preganglionic synapses when these are activated by nerve impulses, and the release also takes place in blood-circulated ganglia. The release occurs only at the synapses and only during synaptic transmission. But from later work reviewed in this discussion it appears that A.Ch. is not regularly released by blood-circulated ganglia, but is released only after a certain departure from normal conditions has been created and then in extremely variable amounts. Synaptic transmission is, therefore, possible without the release of any A.Ch., and also with its release in large amounts. The liberation of A.Ch. is a process that is not specific to the synapses and there are experimental results which indicate that it may take place after transmission has been effected. These recently established facts do not diminish the importance of the discovery of A.Ch. metabolism in sympathetic ganglia and other nervous structures. But they make it advisable to consider whether A.Ch., instead of being the synaptic transmitter, actually plays a less specific role in the course of the electrochemical reactions that take place during transmission of nerve impulses and subsequent processes of recovery.

Rafael Lorente de Nó
The Rockefeller Institute for Medical Research, New York

13 K. Lissák, *Amer. Jour. Physiol.*, 126: 564, 1939.
14 *Ibid.*, 127: 263, 1939.
15 G. L. Brown and W. Feldberg, *op. cit.*, p. 265 ff.
16 K. Lissák, *Amer. Jour. Physiol.*, 127: 263, 1939.
17 O. Loewi and H. Hellauer, *Pflügers Arch.*, 240: 769, 1938.
18 H. Dale, *op. cit.*
19 F. de Castro, *Trav. Lab. Rech. biol., Madrid*, 31: 271, 1936–1937.
20 W. Feldberg and A. Vartiainen, *op. cit.*
21 J. H. Gaddum and W. Feldberg, *op. cit.*
22 G. S. Barsoum, J. H. Gaddum and N. A. Khayyal, *Jour. Physiol.*, 82: 9, 1934.
23 H. Dale, "Harvey Lectures," 229 pp., 1936–1937.

POSTSCRIPT TO "ROGER BACON WAS MISTAKEN"

My brief article in the March 29 issue of Science, though needing no modification, would have been much more illuminating and valuable had it been prefaced by the following statement of facts.

About 20 years ago a heating engineer told me of his winning $2 by betting that a pint of boiling water would freeze sooner than a pint of ordinary drinking water if both pints in similar metal vessels were placed outdoors in zero weather. He had successfully tried this experiment several times before and so was guilty of betting on a certainty. Since that phenomenon seemed to me mysterious I tested it at our physics laboratory and got the same result. The mystery disappeared when I weighed the ice and water in the vessel originally hot and found how much less it weighed than the water in the other vessel. The difference was amazing. This will answer the question asked in the last sentence of Professor Sanford's letter. And in the first sentence of his letter he strangely attributes to me a statement entirely different from the one I made.

The experiment which Professor Lyon performed when a schoolboy disgusted his elders, he says, but they erred in concluding that their experience gained through many years was rendered valueless by a single solitary experiment performed by a youngster. His elders knew that when hot-water and cold-water pipes were near each other the hot-water pipes were generally the first to freeze, but they were unaware of the influence of the air contained in the cold water. In experiments like the one I performed Professor Lyon rightly assigns to evaporation the dominant role. In the experiment which disappointed him he used hot water of unstated temperature. My water was 100° hot.

Professor Wakeham and I apparently disagree only in that while he thinks that both the ancients and Roger Bacon were guilty of generalizing I have too much respect for the intelligence of the ancients to believe them capable of teaching that, although boiling water freezes sooner than an equal weight of lukewarm water, the same phenomenon would be observed in case the colder water was only a few degrees above the freezing point. Professor Wakeham's experiments are of great interest and value, and would be of still greater value had he been able to specify not only the minutes but also the approximate number of seconds in each of his observations. His experiment in which the boiling water at 93.3° and the 20-degree water froze in equal times harmonizes entirely with my experiment in which the 100-degree water froze first. For if Professor Wakeham had been able to start with water boiling at 93.3° and an equal weight of 100-degree water, he would have found that when both masses had come to the same temperature, near the freezing point there would have been considerably less of the 100-degree water than of the other, for in that vessel many more calories had been spent in causing vaporization. Of two unequal masses at the same temperature the smaller freezes first, and consequently Professor Wakeham would have observed the 100-degree water freezing before the 20-degree water just as I did. The 93.3-degree water wasn't quite hot enough to do the trick.

The 2-minute margin of victory of the 10-degree water over the 93.3-degree would have been considerably narrowed, perhaps obliterated, had 100-degree water been at Professor Wakeham's disposal; but a victory should surprise no one, as will appear from the following considerations. As long ago as 1889 Professor Tyndall wrote, "This halt in contraction of the approaching molecules at the temperature of 39° F. (about 4° C.) is but a preparation for the subsequent act of crystalization." Further, it should be kept in mind that water is highly polymerized, a compound of H_2O, $2H_2O$ and $3H_2O$ and that the ratio of these polymers changes with the changes in temperature. According to Rao (1933) 59 per cent. of ice at 0° is composed of $3H_2O$. Also many ice crystals exist in water from 0° to 10° and beyond. With all these advantages it is not surprising that 10-degree water freezes sooner than water boiling at 93.3°.

From the above facts it is clear that not only was the writer of the book from which I quoted ill-advised in denouncing as "drivel" the findings of the ancients, but also that, even ignoring considerations of courtesy in saying "the ancient author was a liar," Roger Bacon was mistaken.

Joseph O. Thompson

Amherst College

A COUNTER-STATEMENT

The statement that follows has been approved by those whose names appear as signers.

In Science for May 3, 1940, there appears an appeal for signatures to a peace manifesto sponsored by the American Association of Scientific Workers. It seems desirable to put on record the fact that this statement does not represent the unanimous opinion of American scientific workers.

One may question whether the manifesto will represent the considered opinion of all its signers, for a casual reading of it might easily fail to disclose its real implications.

It is a platitude that all right-thinking people are, in general, in favor of peace—and the fact is not worth troubling to specify for scientific workers in particular. To lay emphasis on the point now can only be interpreted as implying that in the opinion of the signers our only concern is the re-establishment of peace, regardless of the terms on which it is based.

The manifesto lays emphasis on the importance of the United States keeping out of the war in order to insure