the reason, Verduin's pronouncement "This statement is false" is as erroneous and unfortunate as his allegation that Krogh failed to distinguish between his diffusion constant and diffusivity.

MAX KLEIBER

College of Agriculture,
University of California, Davis

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28 April 1955

In a communication "Diffusion constant and diffusion coefficient" [*Science* **121**, 215 (1955)] J. Verduin criticizes the use of diffusion constants for gases in tissues based on partial pressures (tensions).

Diffusion constants based on partial pressures were introduced by A. Krogh [J. Physiol. **52**, 391 (1919)], who fully understood the difference between a constant so defined and one based on concentration gradients. He choose partial pressures because the absorption coefficients of gases in tissues were—and still are—generally unknown and difficult to determine, which makes the use of concentration-based coefficients impractical in physiological reasoning. Moreover, one of the most important of the diffusion problems of Krogh's time—respiration—necessitates comparison between air and blood, which can hardly be done except on the basis of partial pressure.

Verduin also criticizes Krogh's statement that the diffusion constant as defined by him increases about 1 percent for each centigrade degree increase in temperature. Using the diffusivity and the solubility of oxygen, Verduin calculates the diffusion constant for oxygen in water at 20°C and 30°C as defined by Krogh and finds the values to be 0.346 and 0.338, respectively, which is in contrast with Krogh's statement.

Krogh's statement on the influence of temperature refers, however, to animal tissues and is based on actual determinations that he undertook because the influence of temperature on the solubility of gases in tissues and on the internal friction of the tissues themselves is impossible to calculate.

Krogh was, of course, fully aware that the diffusion rates for the different gases are inversely proportional to the square roots of their molecular weights and of other differences between the constants as defined by him and by the physicists.

Verduin is correct in his statement that the gradient in molecular concentration necessary for the transport of carbon dioxide from the tissues to the capillaries is somewhat greater for carbon dioxide than for oxygen, but translated into partial pressure this concentration gradient is, as Krogh said, absolutely negligible.

It would, of course, be possible to introduce diffusion constants for gases based on concentrations into physiology, but I doubt that it would be practical to give up the use of partial pressures, which for the understanding of the diffusion of gases between alveoli and blood is unavoidable and which we use also in other problems (O_2 dissociation curve of hemoglobin).

However, in order to avoid confusion it would perhaps be useful in every case to state definitely which of the two diffusion constants is used, for example, by denoting the old diffusion coefficient of the physicists—"the Fick diffusion constant" defined as the quantity diffusing through an area of 1 cm² and a thickness of 1 cm in unit time, when the concentration difference is unity—and the one used by the physiologists in the case of gases—"the Krogh diffusion constant" defined as the quantity diffusing through an area of 1 cm² and a thickness of 1 μ/min, when the partial pressure difference is 1 atm.

P. BRANDT REHBERG

Zoophysiological Laboratory,
University of Copenhagen, Denmark

15 March 1955

Ultrasonic Lesions in the Mammalian Central Nervous System

Early histological studies of nerve tissue of animals irradiated with intense focused ultrasound at this laboratory indicated that nerve cell bodies were more susceptible than nerve fibers to changes by the ultrasound (*1*). These preliminary histological results have not been substantiated in subsequent studies. Rather, it has been found, as was previously reported (*2*), that white matter is more readily affected by the sound and that higher ultrasonic dosages are required for producing changes in gray matter. It can be readily seen that this selectivity provides a unique tool for basic neurological studies. Recent publications of this laboratory present results on the production and time sequence of changes in relatively large white-matter lesions of controlled shape (*2, 3*). This paper, however, is concerned primarily with small ultrasonic lesions in both gray and white matter (*4*).

Selective, accurately positioned lesions as small as 2 to 3 mm in maximum diameter can be produced. The lesions, which can be localized at any desired depth in the brain without affecting intervening tissue, are quantitatively reproducible from one animal to another, so that dosage studies made on a series of animals can be used as a guide in choosing the conditions of irradiation for neuroanatomical or functional studies. The blood vessels are most resistant to the action of the sound. It is, therefore, possible to interrupt fiber tracts without destroying neighboring gray matter and without breaking blood vessels even within the site of the lesion. It is also possible, by appropriate choice of the ultrasonic dosage, to affect irreversibly the nerve tissue (fibers and cell bodies) in gray matter without causing hemorrhage.

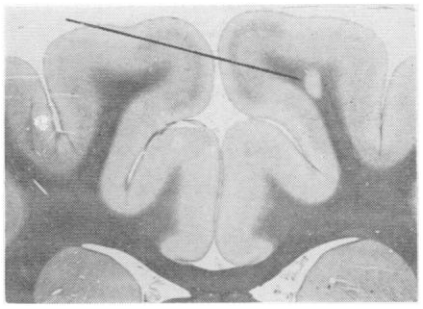

Fig. 1. Small ultrasonic lesion in the subcortical white matter of the brain of a cat. Dosage used selectively affects the fiber tracts, and no damage is produced in the neighboring gray matter. (PTAH stain)

The results reported here were obtained from histological studies of ultrasonically irradiated cats and monkeys. Extensive dosage studies have been completed, and the time course of development of the lesions has been followed in animals sacrificed from immediately after irradiation (5 min) up to 30 days. The preparation of the animal and the technique of irradiation are described in previous papers (*2, 3*). Results of investigations concerned with the physical mechanism of the action of the sound on the nerve tissue have been published (*5*).

When a region of the white matter of the central nervous system is irradiated at one spot with a single exposure of ultrasound at a dosage just above the minimum required to produce an effect, a small lesion about 2 to 3 mm in maximum diameter is produced. Figure 1 illustrates such a lesion in the subcortical white matter 12 days after irradiation (dose 51 atm acoustic pressure and $4.8(10)^3$ cm/sec acoustic particle velocity for 1.00 sec). It shows a sharp boundary between the affected white matter (lower end) and the neighboring unaffected gray matter.

A lesion such as that shown in Fig. 1 is first seen 10 to 15 min following irradiation in tissue sections prepared with Weil's myelin stain. The lesion area is first recognized as a light-staining matrix as compared with normal tissue. One hour after irradiation the myelin sheaths appear beaded. The perivascu-

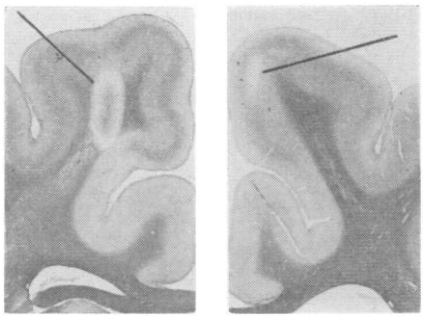

Fig. 2. Ultrasonic lesion in the subcortical white matter of a cat brain exhibiting a central region of dark-staining fibers and some invasion of neighboring gray matter. (PTAH stain) Fig. 3. Small ultrasonic lesion in the cortical gray matter of a cat brain. (PTAH stain)

lar spaces are dilated, and some separation appears between the fibers. Within 6 to 12 hr (depending on the dosage) the myelin sheaths break down into separated spheres. During this same period axis cylinder fragments increase in the lesion area. These changes are followed by the hematogenous and microglial responses until all of the debris is cleared away. Other neuroglia then form a glial scar.

A greater dosage (53 atm acoustic pressure and $4.9(10)^3$ cm/sec acoustic particle velocity for 1.50 sec) produces a slightly larger lesion containing a central normal staining area or island of myelinated fibers surrounded by a zone or moat containing completely disrupted nerve tissue and large clear fluid-filled spaces (Fig. 2). No hemorrhage is present. These more severe lesions may involve neighboring gray matter, causing changes that are described in the following paragraphs. Lesions of the same order of size can be produced in fiber tracts at any depth in the brain without affecting the intervening nervous tissue.

Figure 3 illustrates a small lesion produced by ultrasound in the cerebral cortex of a cat. To produce such a lesion in gray matter, greater dosages of ultrasound are required than for white matter. When a region of gray matter is irradiated with a single exposure at a dosage (53 atm acoustic pressure and $4.9(10)^3$ cm/sec acoustic particle velocity for 2.50 sec) above the minimum required to produce a lesion, the effects that appear first (10 min after exposure) are a lightening in the staining ability of the background matrix and a slight dilation of the perivascular spaces. Nerve cells stain more faintly than normal within 1 hr. Many contain large clear vacuoles in their cytoplasm; others have ruptured cell membranes, and only ragged strands of cytoplasm remain around the still intact nucleus. The nerve cells have disappeared by the end of 1 day. The background contains many clear spaces, and in the more severe lesions large fluid-filled clefts may appear in the tissue. The myelin sheaths and axis cylinders of nerve fibers begin to break down within 1 hr and undergo the afore-described changes for white matter. Some blood-filled capillaries are present at 1 hr. The hematogenous response is manifest within 6 hr by the presence of leucocytes. Microglial multiplication is evident at 4 days, and 12 days after irradiation the glial response is well developed.

The ultrasonic method of producing localized selective lesions in the central nervous system constitutes a unique and potent tool for experimental neurological and neurosurgical applications (*6*). The technique is currently being used in this laboratory in a variety of neurological studies.

W. J. Fry
J. W. Barnard
F. J. Fry
R. F. Krumins
J. F. Brennan

Bioacoustics Laboratory, University of Illinois, Urbana

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11 April 1955

Basic Research versus Pure Research

The recent article by Spaght (*1*) reemphasizes the need for a formalization of concepts concerning words used to describe research and science. Spaght distinguishes between "pure" and "basic" research, although many persons would probably consider the two as equivalent. Spaght's "basic" research is equivalent to the "pioneer," or Edisonian, research as I defined it (*2*).

The current integration of science into the social structure is being highly hindered by the misuse of these and many other terms (*3*). Scientists realize generally that the vocabulary of science must be defined explicitly. Yet many will use terms loosely when they are considering general problems of science. How many scientists could give a satisfactory answer if they were asked to explain what this science of theirs is? Is it any wonder then that nonscientists are confused in their "understanding of science"?

Most efforts in this direction have been made by professional philosophers, to whom much credit is due. Yet the result has been that articles on science, such as those in leading encyclopedias, are almost unintelligible to practicing scientists. Problems and concepts of great importance have been left unconsidered because they could be apparent only to actual research workers.

No criticism of individuals is intended. Spaght and others have the right to define terms as long as no general agreement has been reached. The scientific profession as a whole, however, has been highly lax in developing its own understanding of the general operations and concepts of science.

Is it not time for some scientific organization, such as the AAAS, to assume this obligation? An active committee of representative and qualified persons could do much to expedite the integration of science into society. A possible name might be "committee on the philosophy and social integration of science." Without some such action, scientific research will continue at its organizational level to flounder and to operate highly inefficiently.

Ward Pigman
Biochemistry Department, University of Alabama, Medical Center, Birmingham

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11 July 1955

More on "Unpublished" Material

The recent attention in *Science* to the problem of citing unpublished material in scientific literature prompts me to applaud.

As an editor in the field of the medical and public health sciences, I would like to add to the accumulation of data on this subject. *Public Health Reports*, official journal of the U.S. Public Health Service, 3 years ago began to insist of its authors that all citations and bibliographic references must be published material.

On occasion, if an author properly qualifies a personal communication to the satisfaction of the editors, he may include it in his text but not in the bibliography. We feel rather strongly that no bibliography should contain material inaccessible to the student and researchers. I find no difficulty in concurring with editor Daniel I. Arnon in his summation [*Science* **121**, 835 (1955)] of the case against the personal communication in reviews.

Taft S. Feiman, *Managing Editor Public Health Reports, U.S. Public Health Service, Washington, D.C.*