who was invited to attend the London meeting of the CSSR was also prevented by passport difficulties from going. The readers can judge for themselves what sort of impression our European colleagues must have formed of the importance which our State Department attaches to international scientific conferences. (BART J. BOK, *associate director, Harvard Observatory.*)

Current interest in the therapeutic use of cytochrome C is widespread as a result of a series of papers by S. Proger and associates (*Science*, October 25, 1946, pp. 389–390; *J. clin. Invest.*, 1945, **24**, 864). In an attempt to provide a rational basis for their therapeutic studies, these workers drew certain conclusions which we feel are unjustified. It is understandable that such erroneous conclusions could be drawn, but it is undesirable to have them go unchallenged. The points at issue are as follows:

(1) Proger, *et al.* stated (*Science*, October 25) that "the organs normally contain considerably more cytochrome oxidase than can be activated by the cytochrome C present," based upon our data for cytochrome C content of organs (V. R. Potter and K. P. DuBois. *J. biol. Chem.*, 1943, **142**, 416) and cytochrome C requirement for *in vitro* assay of cytochrome oxidase (W. C. Schneider and V. R. Potter. *J. biol. Chem.*, 1943, **149**, 217). This conclusion is not permissible because the amount of cytochrome required in the assay system is not an indication of how much is needed in the cell and was not intended to be. Proger, *et al.* apparently overlooked the fact that the substrate for cytochrome oxidase is *reduced* cytochrome C, and that the amount of *reduced* cytochrome available to cytochrome oxidase is a function not only of the total cytochrome C present but of the *rate of reduction*. In the assay system this reduction is nonenzymatic and slow; hence, large amounts of cytochrome are used. In the cell the reduction is enzymatic. *Thus, there is no evidence to indicate that cytochrome oxidase needs more cytochrome C than it has available in the cell.*

(2) Proger, *et al.* stated in both articles cited that the cytochrome content of blood and organs was increased following cytochrome C injection. The method used was that of Potter and DuBois. This method does not permit one to decide whether the cytochrome C has penetrated to the inside of the cells or whether it is in the blood and tissue spaces, and was not claimed to do so. In uninjected animals the blood does not contain cytochrome in significant amounts, but this is obviously not the case in the injected animals. *Thus, there is no evidence that injected cytochrome C reaches the interior of the cells.*

(3) Proger, *et al.* also stated that the addition of cytochrome C to homogenized tissue caused increases in oxygen uptake, and concluded that similar amounts of cytochrome C would produce comparable increases *in vivo*. But we have repeatedly emphasized the fact that when a tissue is homogenized, the cytochrome is "diluted" to an extent that depends upon a variety of factors; the extent of the dilution determines the extent of the "stimulation" when cytochrome C is added back. In the intact cells, the cytochrome C is apparently localized in the particles that contain cytochrome oxidase (W. C. Schneider, A. Claude, and G. H. Hogeboom, to be published). There has been no demonstration that the stimulation of oxygen uptake by cytochrome additions observed in homogenates can be duplicated *in vivo*, although the possibility remains that the factors which are concerned in the dilution of cytochrome in homogenates may occasionally operate *in vivo*.

(4) Proger, *et al.* (*J. biol. Chem.*, 1945, **160**, 233) reported that cytochrome C administration prevented the anoxic depletion of the high-energy phosphate reservoirs of the tissues. To me, this experiment would be decisive if it could be confirmed. Unfortunately, the original experiment was done without the precautions that are necessary to preserve the phosphate compounds (G. A. LePage. *Amer. J. Physiol.*, 1946, **146**, 267), and Scheinberg and Michel (*Science*, April 4, pp. 365–366) have failed to confirm the observation.

(5) There remains the final test, clinical benefit, which we are in no position to judge. We have been advised of two unpublished studies with experimental animals that gave negative results. It is desirable that the findings of Proger, *et al.* be tested by some disinterested group as soon as possible in order to prevent a great deal of unnecessary duplication of effort. At present nearly every major pharmaceutical house is undertaking to prepare cytochrome C. It is not the function of these companies to referee conflicting reports, and if the demand for cytochrome C continues, it will be met. But the demand is not a proof of efficacy.

(6) Finally, it must be noted that sound clinical results will stand regardless of their theoretical basis. It may be that cytochrome C will prove beneficial for reasons as yet unknown. (VAN R. POTTER, *University of Wisconsin Medical School.*)

[The above comment was sent by the author to Dr. Proger for criticism before being submitted for publication. Dr. Proger's reply will appear in next week's issue.]

The unfertilized egg of an oyster is pear shaped. In the ripe, unspawned ovary the eggs are tightly packed and compressed. The diameter of the rounded portion of an egg in the oysters kept at Woods Hole is about 40 μ. Assuming that the egg is a sphere, its volume is equal to $\frac{4}{3}\pi R^3$, or $1.33 \times 3.1416 \times 8{,}000$ μ. The volume of 100,000,000 eggs is therefore only 3.3 cc. A certain correction, probably not exceeding 20 per cent, should be added to this figure to account for the void spaces between the eggs. Since the volume of the body of an adult female oyster (without the shell) varies from 15 to 25 cc., the estimated volume of eggs discharged in one spawning is not unreasonable, for it is known that the oysters lose a considerable portion of their body weight after the discharge of sex products.

In the past, too much significance was given to the number of eggs produced by females. Studies conducted by the U. S. Fish and Wildlife Service show that in Southern waters the spawning season extends from early May to October. It is therefore quite possible that the growth of the ovocytes is a more or less continuous process. This point requires further studies which are being conducted at present by the U. S. Fish and Wildlife Service. Potential fecundity of the oyster has, however, little bearing on the success or failure of reproduction, the latter primarily depending on the survival of the oyster larvae rather than on the initial abundance of spawned eggs.

I believe this brief note answers Mr. Burkenroad's criticism of my paper (*Science*, September 26, p. 290). PAUL S. GALTSOFF, *U. S. Fisheries Station, Woods Hole, Massachusetts.*)