tremely brief mention of White's position was "very faulty." If fault there is, it is only in my failure to specify culture; I thought this sufficiently implicit when *ethnologists* were specified. Leeds affirms that "for virtually all propositions in the analysis of culture or culture history, genetic constitutions of individuals . . . can be taken as constants." The difference between that and the view I ascribed to White is subtle, to say the least. In fact White has also maintained that current biological evolution in man is insignificant. Even if unduly succinct, my statement is an inescapable conclusion from White's two propositions. (Nothing was ascribed to White about human evolution in the past.)

The greater part of Leeds's long communication is devoted not to my alleged sin of misstatement but to defense of White's position. That is quite irrelevant to the review that Leeds is ostensibly discussing. I was reviewing Dobzhansky, not White, and extended discussion of my own views on White or other ethnologists did not belong in the review. Even less does it belong in this letter. The points that Leeds here raises are discussed, judiciously and at length, in Dobzhansky's book, to which I urgently refer both Leeds and the readers of *Science*. If Leeds's polemic has made anyone curious as to opinions apparently imputed to me but *not* expressed in the review, I might add that I agree substantially with Dobzhansky.

GEORGE GAYLORD SIMPSON
Museum of Comparative Zoology,
Harvard College,
Cambridge, Massachusetts

Conversion of Pyruvate to Lactate in Tumors

In their article on the pathways of intracellular hydrogen transport (*1*), Boxer and Devlin mention the observations of Busch (*2*) that injected labeled pyruvate was primarily converted to lactate by tumor tissues, in contrast to findings in a number of normal tissues, and that, in experiments with tissue slices, the percentage of added pyruvate that was converted to lactate increased in the presence of added glucose in tumors but not in normal tissues. The explanation was offered that increased flow through the glycolytic pathway requires increased oxidation of reduced diphosphopyridine nucleotide. However, Jedekein and Weinhouse (*3*) and

Glock and McLean (*4*) failed to find any increase in the DPNH/DPN ratio in malignant tissues. The reason for this is clear when it is recalled that for every molecule of diphosphopyridine nucleotide that is being reduced, one molecule of pyruvate is formed concurrently.

A different explanation for this discrepancy could be based on the findings of Bloch-Frankenthal and Ram (*5*) that the oxidation of lactate and pyruvate in tissue slices is inhibited by the addition of glucose. In the opinion of these authors this inhibition occurred at the level of the oxidative decarboxylation of pyruvate.

It may be of interest to relate these observations to the theory of Burk and his co-workers (*6*) that the primary biochemical lesion in cancer cells—or, more correctly, the proximal cause of the aerobic glycolysis of these—is at the site of glucose absorption rather than, as has long been maintained (notably by Warburg), at the oxidative phase of cell respiration. Two different findings are also in accord with this theory: (i) the finding that a lesser degree of malignancy in a chrysoidin induced hepatoma (*7*) that exhibited normal glucose-6-phosphatase activity and was thus able to discard any excess glucose, and (ii) the observation (*8*) that the total incidence of cancer in diabetics is half the incidence in nondiabetic patients.

E. T. RAKITZIS

47 Mouson St.,
P. Phaleron, Greece

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Rakitzis suggests that a discrepancy exists between the extensive conversion of pyruvate to lactate and the observation of essentially normal DPNH/DPN ratios in malignant cells. Hohorst *et al.* (*1*), however, have demonstrated that the ratio of DPNH/DPN is apparently affected by the oxidation-reduction state of the cell and is only one of a number of possible oxidation-reduction pairs. Thus, the rate of glycolysis and of the conversion of pyruvate to lactate does not necessarily control this ratio.

Bloch-Frankenthal and Ram (*2*) sug-

gested that the glucose inhibition of pyruvate utilization in ascites cells was caused by a combination of substrate competition and inhibition of respiration (the Crabtree effect); they proposed that the latter effect of glucose was on the decarboxylation of pyruvate. More recent studies indicate that the mechanism of the Crabtree effect which occurs in malignant tissues as well as in some normal tissues, involves the availability of adenosine di- or triphosphate or inorganic phosphate (*3*), and that the effect is not primarily due to a specific inhibition by glucose.

Rakitzis supports the concept that the cause of the aerobic glycolysis of malignant tissues is at the site of glucose absorption, and he cites the low incidence of cancer in diabetics (*4*) as evidence. In regard to this suggestion a quotation from Bell's paper deserves attention: "It appears that the total incidence of cancer in males over 40 years of age is about twice as large in non-diabetic as in diabetic cases, and in females there is an even greater preponderance in the non-diabetic cases. This is to be expected since every disease which shortens life shows a decreased incidence of malignant disease. The total incidence of cancer is likewise greatly reduced in tuberculosis, heart disease, and cirrhosis of the liver."

GEORGE E. BOXER
THOMAS M. DEVLIN
Merck Institute for Therapeutic Research, Rahway, New Jersey

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Probability Learning

In a report in *Science* (*1*), S. H. Revusky criticizes certain procedures ("forced trials" and "correction") which have been used to control the distribution of reinforcement in experiments on probability learning. With rats trained by Revusky's own ("nonreinforced trials") procedure choosing the more frequently reinforced side of a T-maze on 67.2 percent of trials in what may seem to be a conventional 67:33 probability-learning experiment, the casual reader is apt to gain the impression (i) that probability matching has been demonstrated in the rat, and (ii) that previous failures to demonstrate it may be attributed simply to faulty procedures. Neither of these conclusions would be justified.

Has Revusky demonstrated "probability matching" in the rat? Not in the usual sense of the term (*2*). Nor has he even given us an experiment on "probability learning" in the original (*3*) and still current (*4*) sense of *that* term, which implies a random or quasi-random schedule of reinforcement. The schedule used by Revusky is far from random, and a corresponding nonrandomness appears in the behavior of his animals. Examination of the protocols (*5*) shows, not the gradual emergence of a stable 67-percent preference for the more frequently reinforced alternative (as Revusky's mean values suggest), but a considerable amount of perseveration in one or the other choice—long runs of the preferred response *m* separated by somewhat shorter runs of the alternative response *l*. The tendency toward perseveration may be seen in the choices of one of the animals on the