Communications

Tests for Photoreactivation in Gametes of *Urechis caupo*

Ultraviolet-induced injury to the sperm of the sea urchin, *Arbacia punctulata,* is not reversed by subsequent illumination with visible light, although eggs are readily photoreactivated (*1*). Since the point is one of considerable theoretical interest, it seemed desirable to compare photoreactivation in the gametes of another animal. Studies were therefore made on the sperm and eggs of the echiuroid worm *Urechis caupo* for a comparison of photoreactivation in these gametes.

The worms were collected in Elkhorn Slough on Monterey Bay, California, and kept in running sea water. After withdrawal from the gonosac of the worm, the sperm were diluted 1:400 in 0.05*M* glycine (*2*) in sea water, but the eggs were kept in sea water. By running sea water around the syracuse dishes containing the eggs or sperm, all samples were kept at 16° ± 2°C. Only combinations of gametes giving 90 to 95 percent fertilization and good development were used for experiments. The appropriate gametes were exposed to the radiations of a Sterilamp (mainly wavelength 2537A), the dosage being determined by a Hanovia UV meter. Photoreactivation was accomplished with a G.E. CH-4 Mercury Spotlamp 2 ft from the samples and filtered through 2 to 5 in. of water and a Corning No. 3060 filter to remove heat and ultraviolet radiations, respectively. A 1-hr exposure to the white light alone was not injurious to either sperm or eggs, although it is injurious to the sperm of some animals (*3, 4*). The samples were stirred by playing a jet of air on the surface of the water. The time required for 50 percent of the zygotes to reach the two-celled stage was used to measure the effect of the different treatments, and each of the experiments was repeated at least three times.

Eggs irradiated with a dosage of 3000 erg/mm² of UV and fertilized with normal sperm were delayed in cleavage, a span of time 32 percent longer than the controls being required for half of the eggs to reach the first division. When ultraviolet-injured eggs were treated with white light for 15 min, the delay was reduced by 64 percent, indicating an average of 64 percent photoreactivation. The results were comparable, whether the eggs were illuminated before or after fertilization with untreated sperm.

Dosages of UV from 40 to 480 erg/mm² had no effect on sperm, since eggs inseminated with them were fertilized and cleaved at times comparable to those of controls. Only 50 percent of the eggs were fertilized with sperm given a 3200 erg/mm² dosage of UV, and cleavage was delayed. Sperm subjected to UV dosages of 6400 to 12,800 erg/mm² were generally incapable of fertilizing eggs, only a small percentage of the eggs being activated. These ultraviolet-induced injuries were in no case reversed by illumination with white light; in fact, the injuries were exacerbated. The sperm of *Urechis,* therefore, resemble those of *Arbacia* (*1*) in being incapable of photoreactivation by white light after ultraviolet-induced injury.

Since the possibility exists that a maximal amount of photoreactivation is achieved by the visible light present as an impurity in the spectrum of the Sterilamp, the UV used for irradiating sperm was passed through a visible-light-absorbing filter (*5*) ($CuSO_4$ and $NiSO_4$), which transmits about 70 percent of the UV at 2537A. The results were essentially the same as in the afore-described experiments. Ultraviolet-induced injury to the *Urechis* sperm nucleus therefore appears to be irreversible and is not susceptible to photoreactivation under the conditions tested.

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21 June 1954.

Remarks on Fischer's Article, "Stress and the Toxicity of Schizophrenic Serum"

We wish to put on record some facts concerning the investigation of Roland Fischer (*1, 2*) and to state our disagreements with his conclusions. Fischer acknowledges that his work with *Xenopus laevis* tadpoles was *started* under the direction of one of us (F. G.); but since his published figures are identical with those that he summarized in our laboratory in 1949–50, we are driven to believe that they form the sole basis for his conclusions. We regret that Fischer failed to communicate with us before publishing his paper and that we are thus obliged to object in print to his interpretations:

1) After reexamining statistically all the experimental material, we came to the conclusion that, despite considerable differences in some individual experiments, the results as a whole are *not significant.* This opinion together with other biological experiments has recently been published by one of us (H. P. R., *3*).

2) In this acticle (*3*) no mention is made of Fischer's hypothesis that sudden changes in cold and warm weather would influence the results. In order to survey the extremely complex material, we divided the experiments into three groups: positive, indifferent, and negative, according to the hypothesis under discussion, that schizophrenic body fluids are more toxic than normal ones. Admittedly, a comparison of the

results of the experiments that Fischer reports as having been done under "homogeneous" and "inhomogeneous" weather conditions, on the basis of their biologically positive, indifferent, and negative outcomes, yields a somewhat lower average value of toxicity (with schizophrenics *and* normal controls) for the group of experiments in "inhomogeneous weather." However, the relationship of positive to indifferent to negative findings of 6 : 5 : 2 (or, in percentages, 46 : 39 : 15) is just as good as the one in "homogeneous weather," namely, 22 : 22 : 12 (percentages, 39 : 39 : 21). Thus, while not excluding the possibility of an influence of the weather, it must be stated that the reported experiments do not demonstrate it.

3) We agree with Fischer's statement that serum inactivated by heating is slightly less toxic, but this applies equally to schizophrenic, other pathologic and normal control serums. Experiments with dialyzed serum were ambiguous; some dialyzed serums, but by no means all, were somewhat less toxic than the undialyzed serums, which in most cases unfortunately were very little toxic to begin with.

In these schizophrenic serums, a toxicity in the dialyzate could not be seen, whereas just two dialyzates of normal serums showed considerable toxicity. While these results may be accidental, they certainly do not provide evidence of a dialyzable principle specific for schizophrenia.

4) Fischer seems unaware of the fact that the results of his short series of double-experiments are variable: he overlooks differences up to 8 toxicity units from sample to sample under identical conditions with an average standard error for a single experiment of $\sigma \pm 2.5$ toxicity units at least, and this in "homogeneous weather"! Detailed statements concerning a correlation between toxicity and psychic status of the patient, or conclusions from one or two experiments only, as drawn by Fischer in the cases of hyperemesis, cirrhosis, carcinoma, or pregnancy, are therefore unwarranted.

5) Calculating a "0.001 level of confidence" from an arbitrarily selected group of experiments is not justified, considering that some patients with extremely high toxicity indices figure several times in Fischer's data (see, for example, Rieder, patients 1 and 2, Table 1), whereas others on account of unproved influences are omitted. As was pointed out by Rieder (*3*), differences between normal controls and schizophrenics as a psychiatric group must be evaluated on the basis of the number of *patients* investigated and not on the basis of the number of experiments repeated on these patients with unequal frequency.

Our main contention is that the *Xenopus* method is unsuitable for the detection of the toxic factor in the body fluids of schizophrenic patients (*3*).

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In the foregoing remarks, Georgi *et al.* examine the data of my earlier experiments under a *new* aspect; that is, they disregard the question of whether the results were obtained under controllable, reproducible conditions; then they introduce further statistical analysis. The note of Georgi *et al.* is based mainly on their disregard of the influence of a weather front factor without disproving its existence. I refer, therefore, to another paper of mine that brings further evidence to show how major frontal changes are operative in our biological experiments (*1*).

It is unfortunate that my former associates were unable to grasp the main conclusion of my paper under discussion (*2*) that "the toxicity to tadpoles of serum" of different diagnostic groups "seems to be positively correlated with the degree of stress." In contradistinction to what seems to be the opinion of Georgi *et al.*, I have made no claim whatsoever of a toxic factor specific for schizophrenia (*2*).

The serum and urine toxicity studies under discussion were initiated, designed, and performed under my supervision. I would have expected that Georgi *et al.*, having recently "reevaluated" part of the data I left behind 4 years ago, would have communicated with me before publishing their "main contention that the *Xenopus* method is unsuitable for the detection of the toxic factor in the *body fluids* of schizophrenic patients." I am sorry that I must challenge their unsubstantiated generalization.

That tadpoles at large are suitable test animals to detect the toxicity of schizophrenic serum was already shown by Lazell and Prince (*3*). With the tadpoles of *Rana catesbiana* they demonstrated a toxicity of schizophrenic blood serum tenfold to that of normals. Also, Malis (*4*) was able to show a significant difference in the toxicity of the blood of acute schizophrenics if compared with the blood of normal healthy controls; his test animals were tadpoles of *Rana temporara*.

With the aid of *Xenopus* tadpoles, I could detect one of the main toxic factors in the *urine* of schizophrenics: ammonia (*1*).

If Georgi *et al.* had considered that the more acidic urine of schizophrenics (*1*) contains more ammonia [owing partly to the higher protein catabolism, decreased appetite, and so forth (*5*) of these patients], Weber, under the direction of Georgi, would not have published the papers (*6, 7*) showing that preparations of some 50-liter portions of schizophrenic urine contained more of a mobile ion as measured by ionophoresis. However, "the high toxicity" as measured by their paramecia-test "clearly excludes ammonia, monomethylamine and dimethylamine as the cause," *sic* Weber (*7*). Apparently the paramecia-test method of Georgi *et al.* is unsuitable and caused them to overlook

such a "banal" (*sic* Weber) toxic factor as, for example, ammonia.

Hence it is important to distinguish clearly between specific and nonspecific changes that occur during physiologic or pathologic processes (*5*). For example, it can be shown that the "toxin" present in the urine of menstruating women (*8*) is due mainly to increased amounts of ammonia (*9*), a concomitant of menstrual acidosis. Furthermore, acidosis, a banal change, can produce a decrease in cerebral blood flow (*10*).

Summarized: tadpoles, and especially those of *Xenopus levis,* are reliable test animals, for example, for the detection of a toxic factor in the body fluids of schizophrenics. It is self-evident that the foregoing holds only if one is able to control the conditions under which the experiments are reproducible (*1*).

Finally, I wish to thank Georgi *et al.* for having initiated by their remarks a further clarification of some of our divergent views.

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6 August 1954.

More on "Different IQ's for the Same Individual"

In their independent and valid criticisms of Dreger's study (*1*), Stanley (*2*) and Kurtz (*3*) failed to mention four other highly pertinent considerations.

Perhaps some readers will not recall Dreger's paper. Ten children were each tested on four different intelligence tests, with alternate forms somtimes used. Because numerical IQ's on the same individual "do differ from one another," since there was only one statistically significant correlation between the tests, and because of a significant difference in IQ's as determined by an indefensible method (see criticism by Stanley and by Kurtz), Dreger concluded that "individual's IQ's may differ widely and significantly from one another on different tests." My four additional points of criticism are as follows:

1) It has long been known that numerical IQ's for the same person on different tests may differ because of over-all differences in means and standard deviations and because the tests tap somewhat different functions.

2) The six correlations reported by Dreger are actually based on N's of 9, 5, 7, 6, 7, and 4. Such small N's do indeed aid one in accepting the null hypothesis.

3) Pearson (*4*) as long ago as 1903 demonstrated that correlations are reduced by homogeneity or restriction in range, yet 50 years later we find Dreger drawing conclusions from correlations based on scores that are restricted mainly to average and up (only 5 percent are below average, and not much below at that).

4) Why did Dreger ignore the literature? A quarter of a century ago Goodenough (*5*) reported an r of .74 (N = 334) between the 1916 Stanford-Binet and her Draw-a-Man-Test. Wallin (*6*) reported an r of .72 (N = 290 clinic cases) between the 1916 Stanford-Binet and Arthur I, and an r of .53 (N = 172 clinic cases) between the 1937 Stanford-Binet and Arthur I (contrast this with the r of −.41 given by Dreger on five cases!) Cohen and Collier (*7*) found an η of .71 (N = 51) for the 1937 Stanford-Binet versus Arthur II, and for the same tests Hamilton (*8*) found an r of .73 (N = 40), and Manolakes and Sheldon (*9*) found an r of .64 (N = 217 atypical cases: good and poor readers).

We are forced to agree with Kurtz' conclusions that "Dreger's little study has, thus, contributed nothing. . . ." We also agree with Dreger when he concludes that IQ's from different tests are not comparable, but the lack of comparability is not nearly so sad as he would have us believe. We venture the opinion that Dreger, in his reply (*10*) to Stanley and to Kurtz, missed the point of their criticism. We hope that his hope to repeat the experiment is not realized if by repeat he means an exact replication.

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7 June 1954.

McNemar's criticism (like Kurtz') of one portion of my statistical treatment is correct. I called it "the most indefensible statistically," although I tried to give justification both logically and statistically. In respect to McNemar's specific points:

1) Yes. I cited only two references of the vast literature on test comparisons. Certainly, these other studies emphasizing tests serve as background for work like mine on intra-individual comparisons.

2) If Binet Forms M and L are considered comparable, N's are then 10, 6, 8, 6, 8, and 4. I used Kendall's (*1*) rank correlation coefficient τ, not Pearson's r. The experiment obviously was not intended as a mass demonstration among tests but, instead, to see how *indi-*