Technical Papers

Stress and the Toxicity of Schizophrenic Serum[1, 2]

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Recently (*1*) attention was drawn to a similarity of pathophysiological, as well as psychopathological phenomena, occurring on the one hand, during the course of the schizophrenic process, and on the other, during certain stages of the General Adaptation Syndrom (GAS) of Selye (*2*). In a deliberately oversimplified assumption I put forth the hypothesis that certain phases of the GAS seem to be permanently present during the schizophrenic process, mainly on account of the genetically inherited (*3*) abnormally low threshold of the schizophrenic toward stress. It seemed, therefore, interesting to investigate whether a humoral factor, e.g., a toxic metabolite, might be involved in the release and maintenance of the schizophrenic process.

The serum and urine of acute schizophrenics was tested on larvae of *Xenopus levis* Daudin bred at 20° C. Ten to twenty milliliters/liter of serum or 25–50 ml/l of urine, if added to the water milieu of 14-day-old larvae, caused a significantly higher mortality than the serum and urine of healthy controls in the same dilutions. Longitudinal studies revealed a parallelism between psychical status of the patients and toxicity of their serum and urine, respectively. Spontaneous remission or successful treatments gradually diminished the toxicity near to normal values.

The degree of toxicity is expressed by the mortality of larvae in a certain medium, e.g., serum in water, during the course of an experiment. The mortality is defined as an average of the reciprocal lifespan of a single test animal during a 10-day period; larvae surviving that period are considered as living infinitely long, i.e., with the reciprocal time of zero.

A representative sample of a group of 15 normal healthy control individuals (females and males of the age group 20–35) display a toxicity index of 3.3 and 1.2 in the 20 ml/l and 10 ml/l serum concentrations, respectively. The corresponding values for a group of 12 nonchronic schizophrenics (females and males of the same age group as above) irrespective of their status, treatments, and the effect of their treatments, are 8.1 and 5.3, respectively. The differences in toxicity between schizophrenics and normals are significant at the 0.01 and 0.001 level of confidence for the 20 ml/l and 10 ml/l serum in water experiments, respectively. The differences are, of course, more striking if the serum of acute, untreated, schizophrenics is tested and compared with the serum of normal volunteers.

The toxicity of serum of schizophrenics disappears after exposure to 56° C for 30 min, or after dialysis, whereas urine maintains its toxicity even after being boiled for 30 min.

However, the difference in toxicity between the serum of schizophrenics and normals becomes insignificant on days characterized by a sudden change in warm or cold weather front. This might be related to the stress situation caused in certain normals by front changes. Such meteorotropic stress was related to an increase in 17-ketosteroid excretion (*4*) and would account for the fluctuating index of toxicity of our sera under the above experimental conditions. Acute schizophrenics, however, react differently to meteorotropic and other alarming stimuli. This can be understood if we assume that this group is already under undue stress as a consequence of the schizophrenic process (*1*).

The corresponding indices of toxicity seem to support such a hypothesis since the serum of normal and schizophrenic groups display the same average toxicity, i.e., 2.4 (average of the 20 and 10 ml/l values) if the beginning of the tadpole experiments fall within the 24-hr range before and after sudden front changes.

The above speculation might also be supported by experiments carried out during homogeneous weather and showing an increased toxicity on tadpoles of the blood of normal women with hyperemesis gravidarum in their early stages of pregnancy, or of normal women in their last months of pregnancy. Both of these conditions are also stress situations but apparently less strong ones than represented by the acute catatonic phase. Consequently, the toxic action of the serum, during hyperemesis or late pregnancy, is definitely less pronounced than is the toxicity of blood from acute schizophrenics in the catatonic phase. The hyperemesis patients display a slight increase in toxicity if compared with healthy controls, whereas the toxicity indices of females in their last months of pregnancy lie between the indices of nonpregnant normals and acute schizophrenics. The serum of patients with cirrhosis or carcinoma of the liver shows also similar medium-values.

Thus, the toxicity to tadpoles of serum seems to be positively correlated with the degree of stress, suggesting that an intermediate regulatory mechanism might be connected with the changes in toxicity. The following data seem to support our theory with some further indirect evidence. When dividing a group of normal volunteers into female and male subgroups

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and comparing their indices of toxicity, a fairly constant difference can be found; the 20 and 10 ml/l serum in water toxicity index is 3.0 and 0.4 for females, whereas the corresponding values for men are 3.7 and 1.1, respectively. It is probably not going too far to connect the higher indices of serum toxicity in men with their higher daily average 17-ketosteroids excretion if compared with that of women (*5*).[4]

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[4] More detailed information on this and other aspects of the problem are to be considered in a future report.

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Submicroscopic Structure of "Stratum Corneum" of Snakes[1]

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Superficial microstructure of stratum corneum was noted in European snakes by Leydig (*1*), who suggested its use in systematics as an auxiliary character. Picado (*2*) compared this microornamentation in 3 *Crotalinae*; Schöttler (*3*) in 4 species of the genus *Vipera.*

FIG. 1. *Constrictor constrictor amarali* Stull (1932) (L. 1758).

The dorsal scales of members of the family *Boidae* do not present visible microstructure through the optical microscope. Examination by the electron microscope, however, showed a submicroscopic structure of taxonomic value.

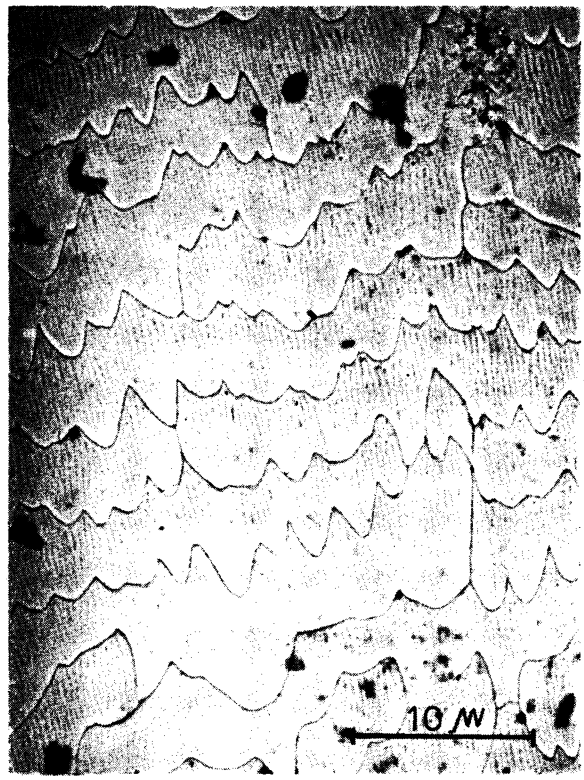

FIG. 2. *Eunectes murinus* L. (1758).

Ten South American species belonging to 5 genera were examined; these included not less than 3 examples of each species, and at least one example of each sex per species. Superficial structure was found in all examples. In addition, a microstructure in the ventral and cephalic shields also could be noted.

Skin fragments with approximately 20 scales were selected from the vertebral mid-body region of adult snakes and washed with acetone. The scales were separated by means of a scalpel, dried, and covered with a 0.5% parlodion solution in amyl acetate. After drying at 50°–60° C, replicas were obtained from the center of the scale by the dry-stripping method (*4*) and shadowed with chromium at an angle of 10°.

Examination of the replicas was made with the help of a Siemens electron microscope, type UM 100b, at 40 kv. Three to four replicas of different scales were examined in order to check the reproducibility of the observed structure. Electron micrographs were taken of representative fields at magnifications of 1300 and

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