

THE INVESTIGATION OF ANTI-RETICULAR CYTOTOXIC SERUM (ACS)¹

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A number of Russian observers have reported promising therapeutic effects in accelerated wound healing, in fractures, skin ulcers, and various pathogenic infections from the use of small "stimulating" doses of the Anti-reticular Cytotoxic Serum (ACS) of Bogomolets (1943). Strauss *et al.* has verified the value of stimulating dosages for fractures of the bones in rabbits (1946*b*) and for fractures in clinical patients (Thompson *et al.*, 1948). The fundamental work of Pomerat and Anigstein (1944, 1945), using tissue culture techniques, and of Miale (1947) with anti-spleen serum in dogs justifies further attempts to check the work reported by the Russian investigators.

Improvements in the preparation of ACS were made. ACS had been previously prepared by the use of tissues from the spleen and bone marrow as antigens (Bogomolets, 1943; Strauss *et al.*, 1946*a*). We discovered (W.M.M.) that bone marrow is unnecessary and that splenic tissue alone produces an anti-cytotoxic serum of high and reliable potency. It was also found desirable to inject the antigen-suspension intraperitoneally rather than intravenously in order to minimize the loss of animals from anaphylactic shock. The antigen could be successfully preserved at -20° C. for an indefinite period of time.

Bogomolets introduced the standardization and control of anti-cytotoxic serums by the use of the complement fixation reaction. To designate the potency of our serums we have used the product of the cubic centimeters and the titer to yield Bogomolets' units (B.U.), *e. g.*, 0.03 cc. of a serum having a complement fixation titer of 1:320 gives 9.6 B.U. In practice the serum is diluted by normal saline solution just before use and injected on a *unit-weight basis only*. This permits complete control of dosage which previously was not done. We have discovered that ACS should only be used on a controlled basis of 0.1 B.U. per kilogram weight of animal or patient.

¹Compiled from the notebooks of Dr. Malisoff collected during his Directorship of the Longevity Research Foundation (dissolved August 23, 1948, by the Supreme Court of the State of New York and all assets transferred to the Robinson Foundation, Inc., 14 Wall Street, New York, which was at that time associated with the work of the Longevity Research Foundation). Through the courtesy of this Foundation the Malisoff notebooks were loaned to the writer for the preparation of this article.

²Deceased, November 15, 1947.

One of our early investigations (1945-6) was on Hodgkin's disease in co-operation with Skapier on the clinical phase. The stimulating dosage schedule recommended by Bogomolets of three graded injections in a few days to yield a series was used. Improvements in the general condition of the patients, increase of body weight, and a more favorable hematological picture were obtained. However ACS was not found to be a cure for Hodgkin's disease. This work was reported in detail by Skapier (1947). The favorable results obtained by using a stimulating dose of ACS are in contrast to the negative results obtained by Abnerthy *et al.* (1948) using blocking dosages.

Our later work on wound healing indicates that it is highly probable even better results would be obtained by single injections of a stimulating dose of 0.1 B.U./kg. about every 20 days. The dosage recommended by the Russian investigators is probably too high (0.2-0.5 B.U./kg) even if used in a series of three graded doses.

Negative results in the wound healing of rats using massive blocking dosages have been reported by Nickerson *et al.* (1946). One of us (W. M. M.) initiated an extensive investigation in co-operation with Maltz, Spain, and Molomut in 1947 (Maltz *et al.*, 1948) on the healing of wounds in mice using over a thousand animals with over two thousand standard wounds. It was found that 0.1 B. U./kg. gave excellent stimulation in wound healing, while 10.0 B. U./kg. gave blockage and complete depressing of the therapeutic action of the mouse ACS. This was followed by several clinical cases on human wounds of long standing which gave rapid, positive and unexpectedly good results.

The program for the systematic investigation of ACS was interrupted after completion of the work on Hodgkin's disease and wound healing in mice.

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A NOTE ON THE CORRELATION BETWEEN NON-
LANGUAGE MENTAL AGES AND READING
TEST SCORES

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designated by a subscript 3. Correlations were: $r_{12}=.59$; $r_{13}=.80$; and $r_{23}=.50$.¹

Only one of the above r 's, that between nonlanguage mental age and reading score (.50), is difficult to account for on logical grounds. Since with an N of 113 the standard error of r when the true r is zero equals .09, the critical ratio exceeds 5 and therefore .50 differs significantly from zero. It hardly seems reasonable on first thought, however, to conclude that nonverbal intelligence *per se* is an important factor contributing to success on a reading test, for all that the two instruments obviously have in common is that they are both paper and pencil tests. Even the formats are quite different.

Considerable light will be shed on the matter if we "partial out" language intelligence by holding constant statistically the influence of language MA and estimating what would be the correlation between nonlanguage MA and reading score if all of these 113 boys had the same language MA. This $r_{23.1}=.06$, not significantly different from zero. Thus there is seen to be no necessity for inferring a *causative* relationship between nonlanguage intelligence and reading ability. Boys with high verbal intelligence tend to have high nonverbal scores also, so the substantial r of .50 between nonlanguage MA's and reading scores stems from this correlation of .59 rather than from factors specific to the nonverbal test itself.

If we were attempting to predict an individual's reading score from some combination of his other two scores, the language MA would be about 18 times as important as the nonlanguage MA. But for predicting language MA from the other two measures the reading score would be approximately $2\frac{1}{2}$ times as valuable as nonlanguage MA. Finally, in predicting nonlanguage MA the appropriate weighting would be nearly 7 for language MA to 1 for the reading score.²

Concomitant variation (co-relationship) should not be mistaken for causation. Frequently the situation can be analyzed as in the above illustration to demonstrate the influence of one or more seemingly extraneous variables.

¹See Ruth Strang ("Variability in reading scores on a given level of intelligence test scores," *J. educ. Res.*, 1945, 38, 440-446), who reports r 's of approximately the same magnitude between scores on the California Test of Mental Maturity, Elementary Form, and four different reading tests administered to children with chronological ages ranging from 96 to 191 months.

²Weightings mentioned in this paragraph would be appropriate only if all measurements were in standard-score form.