sive. Both the bactericidal and tumor inhibitory effects appear to be related to the presence of the —SO—S— linkage and may be the result of —SH inactivation by direct combination or by oxidation of —SH to —S—S—. The decreased uptake of $S^{35}$ L-cysteine by leukemic leukocytes may also be related to —SH inactivation. These effects on malignant cells by an agent which inactivates —SH groups are further suggestive of the importance of —SH metabolism in neoplasia (*10*).

AUSTIN S. WEISBERGER
JACK PENSKY
*Department of Medicine, University Hospitals and School of Medicine, Western Reserve University, Cleveland, Ohio*

### References and Notes

1. F. A. Lehmann, *Arch. exptl. Pathol. Pharmakol. Naunyn-Schmiedeberg's* 147, 245 (1930).
2. C. J. Cavallito, J. S. Buck, C. M. Suter, *J. Am. Chem. Soc.* 66, 1952 (1944).
3. A. Stoll and E. Seebeck, *Helv. Chim. Acta* 31, 189 (1948); 34, 481 (1951).
4. A. Stoll and E. Seebeck, *Advances in Enzymol.* 11, 377 (1951).
5. E. D. Wills, *Biochem. J.* 63, 514 (1956).
6. J. Brachet, *Chemical Embryology* (Interscience, New York, 1950).
7. F. S. Hammet, *A.M.A. Arch. Pathol.* 8, 575 (1929); C. Voegtlin, J. M. Johnson, J. W. Thompson, *U.S. Public Health Repts. (U.S.)* 51, 1689 (1936).
8. L. D. Small, J. H. Bailey, C. J. Cavallito, *J. Am. Chem. Soc.* 69, 1710 (1947).
9. A. S. Weisberger, L. G. Suhrland, R. C. Griggs, *Blood* 9, 1095 (1954).
10. This investigation was supported by a research grant (CY-1678C5) from the National Cancer Institute, National Institutes of Health, U.S. Public Health Service, and was aided in part by the Frederick Sands Memorial Fund and the Cuyahoga Chapter of the American Cancer Society.

3 September 1957

## Biquartimin Criterion for Rotation to Oblique Simple Structure in Factor Analysis

The last 5 years have seen much effort on the part of workers in the field of factor analysis to develop a completely analytical method for rotating axes to what Thurstone (*1*) called "simple structure." Such a method would supplant the largely subjective, graphical methods which have been in wide use for at least 20 years. In 1953 I published (*2*) a method for the general case of oblique axes, but the results were not satisfactorily close to those achieved by the best graphical methods. At about the same time Saunders (*3*), Neuhaus and Wrigley (*4*), and Ferguson (*5*) independently proposed what Neuhaus and Wrigley called the "quartimax" method, which yielded an approximation to simple structure under the restriction of orthogonality. This method is mathematically equivalent to my method, under the stated restriction. Kaiser (*6*) showed that part of my solution can be achieved by the use of a characteristic equation; he also presented (*7*) a further criterion for the orthogonal case, called the "varimax" criterion since it depends on maximizing the variance of squared factor loadings. Pinska and Saunders (*8*) suggested a variant of their criterion for the oblique case, and Kaiser (*9*) generalized his varimax method for the oblique case.

This report (*10*) presents the "biquartimin" criterion for simple structure in the oblique case. When applied to several "school problems" such as Thurstone's box problem (*1*, p. 229), it yields results which appear to be closer to graphical solutions than those yielded by other analytical approaches. The complete evaluation of this and other methods awaits the development of parallel high-speed computational systems and their application to a wide variety of data.

To introduce the biquartimin criterion, it may help to refer to my original method (*2*) as the quartimin, since it depended upon the minimization of the sum of the cross-products of squared factor loadings and thus involved terms of the fourth degree. Let the $n \times m$ matrix of the initial factor loadings be denoted F, where $n$ is the number of variables and $m$ is the number of factors. Then, the quartimin method finds a transformation matrix $\Lambda$ such that it will be true of the elements $v_{jp}$ of the resulting matrix $V = F\Lambda$ that

$$\sum_{p<q}^{m} \sum_{j=1}^{n} v^2_{jp} v^2_{jq} = \text{a minimum},$$

where $j = 1,2, \ldots n$, and $p, q = A,B, \ldots m$. The rationale offered for the quartimin criterion depended on the fact that simple structure requires a maximum number of zero or near-zero entries in V.

Kaiser's (*9*) generalization of his varimax criterion to the oblique case might be called the *covarimin* criterion, since it requires that the sum of the covariances of squared factor loadings be a minimum; that is, that

$$\frac{1}{n} \sum_{p<q}^{m} \sum_{j=1}^{n} v_{jp} v_{jq} = \text{a minimum},$$

where

$$v_{jp} = (v^2_{jp} - \overline{v^2_{jp}})$$

The covarimin criterion is closely related to the quartimin criterion but corrects for the mean value of the squared factor loadings. Thus, the latter utilizes the deviations of squared factor loadings from zero while the former utilizes deviations from their mean value.

Experimentation with the quartimin and covarimin criteria as applied to several sets of real or hypothetical data revealed that the presence of factorially complex variables created almost precisely opposite disturbances, the quartimin axes being too highly correlated and the covarimin axes being too much separated. The centroids of corresponding quartimin and covarimin transformation vectors proved to be very close approximations to the results of graphical solutions, but this type of solution (although otherwise acceptable) was rejected because it would entail more than twice the normal amount of computation and the possibility of difficulty in identifying corresponding vectors.

Table 1. Data for Thurstone's "box problem" (*1*, p. 229): transformation matrix ($\Lambda$) obtained by the analytical biquartimin method as compared with that obtained by Thurstone by graphical methods.

| | X | Y | Z |
|---|---|---|---|
| | *Biquartimin criterion* | | |
| I | .450 | .434 | .473 |
| II | −.862 | .237 | .597 |
| III | .234 | −.869 | .648 |
| | *Thurstone's solution* | | |
| I | .483 | .466 | .479 |
| II | −.834 | .254 | .560 |
| III | .267 | −.847 | .675 |

The biquartimin criterion combines the advantages of the quartimin and covarimin methods by requiring that the expression

$$\sum_{p<q}^{m} \left[ \sum_{j=1}^{n} v^2_{jp} v^2_{jq} + \sum_{j=1}^{n} v_{jp} v_{jq} \right]$$

be a minimum. It doubly satisfies the requirement of parsimony (*5*) in that the sum of cross-products of squared factor loadings must be minimized along with the sum of cross-products of deviations of squared factor loadings from their mean values.

In one of several possible computational schemes, the biquartimin criterion can be expressed as the sum of the off-diagonal elements of a symmetric matrix composed of quadratic forms—that is,

$$\sum_{p<q}^{m} \lambda_p H_q \lambda'_p = \text{a minimum},$$

where $\lambda_p$ is a transformation vector of $\Lambda$ and

$$H_q = 2n \sum_{j=1}^{n} (\lambda_q F'_j F_j \lambda'_q) F'_j F_j - (\lambda_q F' F \lambda'_q) F' F,$$

where $F_j$ is the $j$th row of F. The solution for the minimum value must be made iteratively. For any one stage of the iterations, designate the vector to be solved for as $x$ and any one of the remaining vectors as $r$, then determine

$$\lambda_x (\Sigma H_r) \lambda'_x = \text{a minimum}$$

by determining $\lambda_x$ as the latent vector corresponding to the smallest latent root of the symmetric matrix ($\Sigma H_r$). (In

starting the computations, each of the vectors $\lambda_r$ may be chosen arbitrarily.) In the next stage of the iterations, the $\lambda_x$ just solved for becomes one of the $\lambda_r$'s, and another vector becomes the $\lambda_x$ to be solved for. In the small problems which have been worked thus far, with $m$ no greater than 4, convergence has been reasonably rapid, depending in large measure on the apparent "cleanness" of the factorial structure.

As an illustration of results obtained, Table 1 compares the biquartimin solution with that obtained by Thurstone (*1*, p. 229) by graphical methods for his "box problem." Corresponding transformation vectors from the two solutions are about 3° apart.

The principle utilized by the quartimin criterion could be applied easily to the special case where one requires orthogonality. This has not yet been done; at any rate, it would seem that the criterion of simple structure should alone determine to what extent any given set of data approaches orthogonality. Like other oblique solutions, the biquartimin criterion allows complete freedom in this respect.

JOHN B. CARROLL
*Graduate School of Education, Harvard University, Cambridge, Massachusetts*

### References and Notes

1. L. L. Thurstone, *Multiple-Factor Analysis* (Univ. of Chicago Press, Chicago, 1947).
2. J. B. Carroll, *Psychometrika* 18, 23 (1953).
3. D. R. Saunders, *An Analytic Method for Rotation to Orthogonal Simple Structure* (Educational Testing Service, Princeton, N.J., 1953).
4. J. O. Neuhaus and C. Wrigley, *Brit. J. Statist. Psychol.* 7, 81 (1954).
5. G. A. Ferguson, *Psychometrika* 19, 281 (1954).
6. H. F. Kaiser, *ibid.* 21, 89 (1956).
7. ———, *Am. Psychologist* 10, 438 (1955).
8. C. Pinska and D. R. Saunders, *Analytic Rotation to Simple Structure, II: Extension to an Oblique Solution* (Educational Testing Service, Princeton, N.J., 1954).
9. H. F. Kaiser, "Varimax method of factor analysis," unpublished Ph.D. dissertation, University of California, 1955.
10. I thank Albert E. Beaton, Jr., and Frederic D. Weinfeld for their help in programming the computations for a high-speed computing machine (IBM Type 650). I am also indebted to the John Hancock Mutual Life Insurance Company and to the Statistical Computation Laboratory of Boston University for making computing facilities available. A complete report is in preparation.

19 July 1957

## Chemoprophylaxis with Diazouracil of Poliomyelitis in Mice

One approach to the chemotherapy of virus diseases has been the use of various antimetabolites to interfere with nucleic acid metabolism (*1*). Since the publication of the reports on the action of benzimidazole against poliomyelitis in mice (*2*), investigation of compounds of this nature has been pursued in this laboratory (*3*) as a possible method for chemoprophylaxis. One of the substances tested was diazouracil, which had been found to have some activity against certain viruses (*4*). This report presents evidence about the effectiveness of diazouracil in the prevention of paralytic poliomyelitis in mice.

Table 1. Chemoprophylaxis of poliomyelitis with diazouracil in mice. Mice were inoculated intraperitoneally with an estimated 10 $ID_{50}$ of $MEF_1$ poliomyelitis virus. Diazouracil treatments (10 mg/kg day, intraperitoneally) were given for 4 days, beginning one day before virus inoculation.

| Treated No. surviving/ No. inoculated | Control No. surviving/ No. inoculated | Survival index |
|---|---|---|
| | *Sample No. 1* | |
| 11/19 | 3/20 | 5.0 |
| 6/20 | 2/20 | 2.0 |
| 8/20 | 2/19 | 1.7 |
| 7/19 | 1/20 | 1.6 |
| | *Sample No. 2* | |
| 6/20 | 0/20 | 1.7 |
| 8/19 | 5/20 | 1.9 |
| | *Total* | |
| 46/117 (39%) | 13/119 (11%) | |

In these studies, mice of the Webster strain weighing less than 12 g were inoculated intraperitoneally with 0.2 ml of a 10 percent suckling-mouse brain suspension of the $MEF_1$ strain of type II poliomyelitis virus, approximately 10 $ID_{50}$. Mice were treated intraperitoneally with diazouracil (*5*) at the rate of 10 mg/kg day for 4 days beginning the day before virus inoculation; however, on the day of virus administration, treatment was given subcutaneously. Control animals were treated similarly with equal volumes of buffered saline. Mice were examined daily for paralysis throughout an observation period of 21 days.

Data from several experiments with diazouracil are presented in Table 1. The results are expressed as the ratio of the number of animals surviving on the 21st day to the number of animals inoculated. A survival index was calculated from the ratio of the harmonic mean of the survival time of the treated group to that of the control group, with a favorable response in terms of prevention or delay indicated by ratios greater than 1 (*6*). In all experiments, diazouracil reduced the incidence or delayed the onset of paralysis in mice inoculated with poliomyelitis virus. Thus, in the first experiment, treatment with diazouracil reduced the incidence of poliomyelitis from 85 percent (three survivors of 20 mice inoculated) to 42 percent (11 of 19 surviving), with harmonic mean survival times of 4.0 and 20.2 days, respectively. When the results of these tests were combined, it was found that only 13 of 119 control animals survived, compared with 46 of 117 treated animals—a difference significant at the 1 percent level (*7*). When treatment with diazouracil was begun on the day of virus inoculation or thereafter, it was less effective. No protection was observed when intraperitoneal treatment with diazouracil was started the second day after virus infection or when diazouracil was given orally at the rate of 100 mg/kg day for 4 days beginning the day before virus inoculation.

In contrast to its action in mice, diazouracil did not protect monkeys. When infected orally with the Mahoney strain of poliomyelitis virus, 6 of 6 monkeys in each of two control groups developed paralysis, as did a group which was treated intraperitoneally with four daily doses of 5 mg of diazouracil per kilogram each, beginning the day before virus inoculation, while in a group treated intravenously with five daily doses of 2.5 mg/kg, the morbidity was 5 of 6.

Although the effectiveness of diazouracil is compatible with the assumption that analogs can be used to interfere with the nucleic acid metabolism involved in virus replication, it remains to be demonstrated that this is the mechanism of the chemoprophylactic action of the compound against poliomyelitis in mice.

KENNETH W. COCHRAN
*Department of Epidemiology* and *Virus Laboratory, School of Public Health, University of Michigan, Ann Arbor*

### References and Notes

1. R. E. F. Matthews and J. D. Smith, *Advances in Virus Research* 3, 49 (1955); E. W. Hurst and R. Hull, *Pharmacol. Revs.* 8, 199 (1956).
2. G. C. Brown, *J. Immunol.* 69, 441 (1952); G. C. Brown, D. E. Craig, A. Kandel, *Proc. Soc. Exptl. Biol. Med.* 83, 408 (1953).
3. These studies were aided by a grant from the National Foundation for Infantile Paralysis.
4. D. E. Schlegel and T. E. Rawlins, *J. Bacteriol.* 67, 102 (1954); G. W. Mast, personal communication; C. H. Knox, M. L. Robbins, P. K. Smith, *J. Pharmacol. Exptl. Therap.* 119, 495 (1957).
5. Diazouracil for these studies was generously supplied by the Nepera Chemical Company.
6. R. E. Shope, *J. Exptl. Med.* 97, 601 (1953); K. W. Cochran, G. C. Brown, T. Francis, Jr., *Proc. Soc. Exptl. Biol. Med.* 85, 104 (1954); K. W. Cochran and T. Francis, Jr., *ibid.* 92, 230 (1956).
7. D. Mainland and I. M. Murray, *Science* 116, 591 (1952).

25 July 1957

## New Low Chromosome Number for Plants

Previously, the lowest chromosome number reported for plants was $X = 3$. This number occurs in *Crepis, Crocus,* and *Ornithogalum* (*1*). In the process of a biosystematic study of the *Blepharodon* section of *Haplopappus* several species have been found to have low chromosome numbers. Of particular interest, however, is *Haplopappus gracilis* (Nutt.) Gray. This is a small annual composite that ranges from southern