Combined treatment with HBB and guanidine was, therefore, expected to have a greater suppressive effect on virus reproduction than either compound alone. This proved to be the case in experiments with 'Coxsackie B3' and 'ECHO 5' viruses[5,6].

The large effect of combined treatment suggested, however, that it was not solely due to inhibition of mutants exhibiting limited cross-resistance, but that, in addition, HBB and guanidine acted synergistically.

The following experiment was carried out to test this possibility. 'Coxsackie A9' virus was grown in primary monolayer cultures of rhesus monkey kidney cells in a single infectious cycle[7]. HBB and guanidine hydrochloride, either alone or in combination, were added to the cultures at the end of the viral adsorption period, that is, 1 h after virus inoculation. The cultures were collected 7 h later and virus yields were determined by the plaque technique[7].

Table 1 shows the result of a typical experiment. HBB, 19 μM, or guanidine, 219 μM, had no effect on virus reproduction when given alone. 2·25-fold higher concentrations of HBB or guanidine reduced the virus yield 50–300 times. Yet still higher concentrations of either compound were required to suppress virus reproduction completely. On the other hand, 19 μM HBB and 98 μM guanidine, when given in combination, inhibited virus growth completely. The complete inhibition cannot be explained on the basis of inhibition of mutants resistant to one compound but sensitive to the other, since neither compound was used at inhibitory concentration.

Table 1. SYNERGISTIC EFFECT OF HBB AND GUANIDINE ON THE MULTIPLICATION OF 'COXSACKIE' A9 VIRUS

Compound	Concentration μM	Virus yield: Plaque-forming units/ml.	Virus yield: Treated, per cent of untreated control
None	—	$3\cdot0 \times 10^8$	100
HBB	19	$3\cdot0 \times 10^8$	100
	43	$6\cdot5 \times 10^6$	2·2
	98	$1\cdot6 \times 10^5$	0·05
Guanidine	219	$3\cdot5 \times 10^8$	117
	493	$1\cdot1 \times 10^6$	0·4
	1,110	$1\cdot4 \times 10^5$	0·05
HBB	19		
+ Guanidine	98	$2\cdot0 \times 10^5$	0·07

Two other combinations (29 μM HBB + 219 μM guanidine; 43 μM HBB + 98 μM guanidine) were also found to inhibit virus reproduction completely, and even 9 μM HBB + 98 μM guanidine had some effect (72 per cent inhibition).

The mechanism of the synergistic effect of HBB and guanidine on virus multiplication is not known at present. Both compounds inhibit the production of virus-induced RNA polymerase[8], and of viral RNA and coat protein[7,9–12]. It may, therefore, be hypothesized that the compounds affect different aspects of the virus-specific reaction sequence which leads to the synthesis of viral RNA.

From a practical point of view, combined use of both compounds holds promise for the treatment of virus diseases.

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HANS J. EGGERS
IGOR TAMM

The Rockefeller Institute,
New York 21, N.Y.

[1] Tamm, I., and Eggers, H. J., *Science* (in the press).
[2] Eggers, H. J., and Tamm, I., *J. Exp. Med.*, **113**, 657 (1961).
[3] Tamm, I., and Eggers, H. J., *Second Intern. Symp. Chemotherapy*, Naples, 1961, Part II, 88 (S. Karger, Basle, New York, 1963).
[4] Melnick, J. L., Crowther, D., and Barrera-Oro, J., *Science*, **134**, 557 (1961).
[5] Tamm, I., and Eggers, H. J., *Bact. Proc.*, 139 (1962).
[6] Tamm, I., and Eggers, H. J., *Virology*, **18**, 439 (1962).
[7] Eggers, H. J., and Tamm, I., *Virology*, **18**, 426 (1962).
[8] Baltimore, D., Eggers, H. J., Franklin, R. M., and Tamm, I., *Proc. U.S. Nat. Acad. Sci.*, **49**, 843 (1963).
[9] Eggers, H. J., and Tamm, I., *Nature*, **197**, 1327 (1963).
[10] Eggers, H. J., Reich, E., and Tamm, I., *Proc. U.S. Nat. Acad. Sci.* (in the press).
[11] Holland, J. J., *Proc. U.S. Nat. Acad. Sci.*, **49**, 23 (1963).
[12] Crowther, D., and Melnick, J. L., *Virology*, **15**, 65 (1961).

ANTHROPOLOGY

Selection Intensity in Brazilian Caingang Indians

IT is becoming increasingly clear that if we wish to understand the biological evolution of man we must examine in detail the selective pressures and breeding structures of human populations which are in different stages of cultural development. Crow[1] suggested a relatively simple method for measuring selection intensity in man. This communication describes the results obtained with Crow's method collected from among the Caingang Indians living in the State of Rio Grande do Sul, Brazil.

These Indians have already been subjected to a series of investigations which aim at understanding the evolutionary forces which shaped their present genetic constitution[2,3]. Details about the location of these groups and their demographic structure were described in a previous paper[2].

Table 1. SELECTION INTENSITY IN CAINGANG INDIAN POPULATIONS OF RIO GRANDE DO SUL, BRAZIL

Population	N_1	$\bar{x}$	Vf	N_2	pd	Im	If	I
Ligeiro	24	4·5	16·4	262	0·439	0·783	0·810	2·2
Cacique Doble	15	5·2	10·5	156	0·327	0·486	0·389	1·1
Guarita	46	7·4	14·4	768	0·410	0·695	0·263	1·1
Nonoai	49	6·0	14·4	681	0·417	0·715	0·400	1·4

N_1, No. of women studied whose age was 40 or more; $\bar{x}$, average No. of live births per woman; Vf, variance in progeny number due to fertility; N_2, total No. of live births (women of all ages); pd, premature deaths (died before the reproductive age); Im, mortality component; If, fertility component; I, index of total selection intensity.

The results are shown in Table 1. The average number of live births per woman aged forty years or more varied from 4·5 to 7·4. The corresponding variance was 10·5–16·4. The mortality before the reproductive age ranged from 32·7 to 43·9 per cent. From these results the mortality and fertility components of the index of total selection intensity, Im and If respectively, can be calculated. Im varied from 0·486 to 0·783; If from 0·263 to 0·810. The extreme index values obtained were 1·1 and 2·2. Spuhler[4] has recently reviewed the information concerning these variables in ten tribal populations. The index of total selection intensity varied in these groups from 0·6 to 3·7. The values presented here, therefore, are in the lower half of the range observed. This shows that the Caingang are not subjected to too stringent selective pressures, despite the heavy mortality before the age of reproduction observed among them. In five of the ten populations reviewed by Spuhler the mortality component was higher than the fertility one, while in the five others the opposite occurred. Among the Caingang three of the populations presented higher Im and only one higher If values. Mortality is still very important in determining the gene frequencies in these Indian groups. Total selection intensity is about the same in Cacique Doble, Guarita and Nonoai, but, due to fertility differentials, shows a two-fold increase in Ligeiro.

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FRANCISCO M. SALZANO

Departamento de Genética,
Instituto de Ciências Naturais,
Universidade do Rio Grande do Sul,
Pôrto Alegre,
Brazil.

[1] Crow, J. F., *Human Biol.*, **30**, 1 (1958).
[2] Salzano, F. M., *Human Biol.*, **33**, 110 (1961a).
[3] Salzano, F. M., *Z. Morphol. u-Anthrop.*, **51**, 536 (1961); *Amer. J. Phys. Anthrop.*, **19**, 391 (1961); *Ann. Human Genet.*, **25**, 123 (1961). Tondo, C. V., and Salzano, F. M., *Science*, **132**, 1893 (1960). Salzano, F. M., Marçallo, F. A., Freire-Maia, N., and Krieger, H., *Acta Genet.*, **12**, 212 (1962). Salzano, F. M., and Sutton, H. E., *ibid.* (in the press).
[4] Spuhler, J. N., *Proc. UN/WHO Seminar Use of Vital and Health Statistics for Genetic and Radiation Studies* (United Nations, New York, 1962).