rapid growth is past. Its reproductive differentials are, in general, negatively correlated with social, economic and occupational status. But it is to be noted that these three are not independent variables, but on the contrary correlated with each other. Because of these reproductive differentials the future composition of the population, from whatever point viewed, is likely to be divergent from its present one. On this account the authors are rightly cautious about making predictions. No important differences in reproductive performance are found between large racial or national groups in our population. The authors are soundly skeptical about theories of "optimum population" numbers. "The accumulation of surplus population in agriculture areas with limited natural resources" is looked upon as the most serious economic aspect of present population trends. There is found also a trend towards an increase in families with the background of unskilled laborers in a time when the demand for manual labor is plainly contracting rather than expanding, and is likely to continue to do so with the steady progress in the application of science to all processes of industrial production.

The militant eugenist seems likely to derive singularly little warming or cheering sustenance from this book. For it is found that the only point at which anything like convincing evidence of hereditary differences playing an important rôle in large population groups is in relation to the occupational classification. There are three studies in this field regarded by the authors as worthy of some credence, and they indicate "that from one third to one half of the variations usually found among occupational classes in average levels of cultural-intellectual development are due to deviations in hereditary capacities." After some cautionary reservation about this conclusion the authors go on to state that they regard it as conclusively proved that the apparent differences in cultural-intellectual development between major racial groups are due in large part to environmental rather than hereditary influences. They find it even more true that there appear to be no significant differences in hereditary capacities for intellectual development between large social, or urban *versus* rural, groups. They are also extremely skeptical as to the existence of hereditary differences in vitality (health and longevity) between large groups, either regional, racial or social, admitting at the same time the cogency of the evidence of the importance of hereditary factors in determining inter-individual differences in respect of health and longevity.

The general conclusion of the whole survey seems sound and intelligent.

> Our vast educational program may perhaps be sufficient to outweigh the depressing effects of present population trends in their purely environmental aspects. It can never make up for the dying out of any large proportion of people with superior capacities for education. Two mass tendencies are apparently moving in direct opposition: the conscious force of educational endeavor, and the blind influence of present population drift.
>
> Thus many of the present varying rates of reproduction of American groups are bad from the economic, the cultural, or the eugenic point of view. There is, however, an encouraging indication that present differences in reproduction rates are in part the expression of an incomplete social process; some of the most extreme differentials in fertility among American groups are likely to disappear as current changes in attitudes and behavior, already established in a large portion of the population, spread to more isolated, less privileged, and less developed groups.

The book is a little marred by some minor defects. Perhaps the worst of these is a tendency to unnecessary over-elaboration of the discussions, with repetitions and some confusion of the reader as consequences. Conciseness of statement would have enhanced the value and influence of the treatise. The discussion of theoretical genetics in the latter part of Chapter X seems unfortunate for two reasons, first because unnecessary to the argument, and second because it partakes rather more of the nature of Alice in Wonderland than of objective, natural science. There is displayed in an otherwise well and abundantly illustrated book a somewhat distressing fondness for "pie" diagrams, a form of graphic representation now commonly avoided by statisticians other than those attached to the advertising business.

But these and some other offenses to some tastes and judgments that might be mentioned are, after all, minor faults, in a really excellent and valuable book that will be welcomed and treasured in the library of every serious student of human biology.

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SPECIAL ARTICLES

THE ISOLATION OF CRYSTALLINE TRYPSINOGEN AND ITS CONVERSION INTO CRYSTALLINE TRYPSIN

THE isolation of a crystalline protein, chymotrypsinogen, from acid extract of fresh cattle pancreas and its conversion into an active proteolytic enzyme, chymo-trypsin, has been previously described.[1] The filtrate from the chymo-trypsinogen

[1] M. Kunitz and J. H. Northrop, SCIENCE, 78: 558, 1933.

contains trypsinogen, the inactive form of trypsin, and becomes active upon the addition of enterokinase or upon dissolving in concentrated magnesium or ammonium sulfate.[2] Under the latter conditions the activation is autocatalytic. This trypsinogen has now been isolated in crystalline form as short triangular prisms. It is a protein and has no proteolytic activity but becomes active under the same conditions as does the original filtrate from the chymo-trypsinogen. Thus, on standing in concentrated magnesium sulfate solutions at pH 7.0–8.0 this protein is transformed into the active proteolytic enzyme, trypsin, which may then be crystallized in the form of short rectangular prisms or fine needles. The activation reaction is autocatalytic. The activation curve for the crude trypsinogen solution shows a prolonged lag period due probably to the presence of an inhibiting substance. This prolonged lag period allows crystallization of trypsinogen to take place before activation. The solutions of crystalline trypsinogen, however, activate much more rapidly and there is no lag period. For this reason it has not been possible, so far, to recrystallize the trypsinogen, since the conditions for crystallization are also those for activation. The trypsinogen is, therefore, transformed to active trypsin before trypsinogen crystals can form, and the crystals which later appear are those of active trypsin instead of trypsinogen. Crystalline trypsin obtained in this way is identical, so far as has been determined, with the crystalline trypsin previously isolated from active pancreatic extract.[3]

The method of isolation of these crystalline proteins is briefly as follows. All the solutions used must be cooled to about 5° C. and all operations are carried out in the icebox. The mother liquor from the chymotrypsinogen crystallization is titrated to pH 4.0 with 2.5 M sulfuric acid, brought to 0.7 saturated ammonium sulfate and filtered. 100 gm of the precipitate is dissolved in 300 ml water, brought to 0.4 saturated ammonium sulfate and filtered. The filtrate is brought to 0.6 saturated ammonium sulfate by slow addition of saturated ammonium sulfate and filtered with suction. The precipitate is washed twice on the filter with saturated magnesium sulfate. Ten gm of filter cake is dissolved in 10 ml 0.4 M borate buffer pH 9.0; 17 ml saturated magnesium sulfate is added and the solution allowed to stand at 6° C. Short triangular pyramids appear in the course of 2 to 3 days. If the solution is inoculated crystallization is much more rapid, but the crystals are not so well formed. Occasionally the solutions become active and crystallization stops or crystals of the active trypsin may appear.

[2] M. Kunitz and J. H. Northrop, SCIENCE, 80: 190, 1934.

[3] M. Kunitz and J. H. Northrop, *Jour. Gen. Physiol.* (in press).

CONVERSION OF TRYPSINOGEN TO TRYPSIN AND CRYSTALLIZATION OF TRYPSIN

Trypsinogen crystals are washed with 0.5 saturated magnesium sulfate in 0.10 M borate buffer pH 8.0 and then with saturated magnesium sulfate in 0.1 M acetic acid. Ten gm filter cake is suspended in 5 ml 0.01 M sulfuric acid and 2.5 M sulfuric acid added drop by drop until the crystals dissolve. Ten ml saturated magnesium sulfate and 5 ml 0.4 M borate buffer pH 9.0 is added and pH adjusted with saturated potassium bicarbonate solution to pink to phenol red on test plate. The solution is inoculated and allowed to stand at about 5° C. A heavy crop of trypsin crystals forms in a few hours. The first crystals may be poorly defined. Recrystallization is carried out in the same way but with slightly more dilute solution of the protein. The crystals are needle-shaped and may be quite short or may appear in rosettes. The purified trypsin obtained from active cattle pancreas, as previously described,[3] may be crystallized under the same conditions. Much better crystals are obtained in this way than when crystallization is carried out at pH 4.0 and room temperature with ammonium sulfate, as in the original method.

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