for this discrepancy except by postulating that albinism is determined, not by one recessive gene, but by any one of several.

Retinitis pigmentosa presents the same phenomenon. The percentage of cousin marriages in the Usher⁵ pedigrees, as summarised by Hogben,¹ is also 17. The incidence of the condition, even excluding cases determined by dominant inheritance, must be much higher than 1 in 168,000. It is to be noted that the exclusion of certain cases by Hogben cannot affect the result. The incidence of consanguineous unions is at least as high for the unselected material. This applies to albinism also. Juvenile amaurotic idiocy may be taken as a third example. In Sjögren's⁶ families, the percentage of cousin marriages is 15.3, corresponding to an incidence of the condition in the general population of 1 in 130,000, again an excessively low value.

Alcaptonuria provides an interesting contrast. The data have been recently summarised by Hogben, Worrall and Zieve.⁷ The incidence of first cousin marriages is 42 per cent. This corresponds to an incidence of the defect of 1 in 2,330,000. The figure of 42 per cent may be too high as it is based only on those families in which the relationship of the parents is definitely stated, but the authors point out that even if it were not too high, the figure of 1 in 2,000,000 is probably not too small for this very rare condition.

It seems very probable, therefore, that many human defects may be conditioned not only by one of two or three factors differing in their transmission, but also by one of several factors exhibiting the same type of transmission. The crucial test would be provided by the marriage of unrelated affected persons, but such marriages are, unfortunately, very rare.

The reason why it should so frequently happen in human records that the same end result may be due to one of several factors is not difficult to understand. In laboratory material, or in domesticated animals and plants, the observer is usually dealing with one strain, or with a stock in which inbreeding has taken place. In the case of human defects, on the other hand, countless observers all over the world are constantly putting on record a substantial proportion of the rare deformities occurring in a race in which random mating is the rule.

The implications, if the phenomenon is accepted as one of general occurrence, are of considerable theoretical and practical importance, but it is unnecessary to discuss them here. The value of studies on consanguinity is emphasised especially in the case of conditions that are too common for a significant excess to be expected if only one factor were concerned. It is also becoming increasingly evident that an adequate human genetic prognosis demands a close study of the individual family concerned against the background of cases recorded in the literature, these being sifted, classified and analysed by appropriate methods.

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Evolution of Hormones

It is clear that the integrative mechanism implied in the word 'hormone' or its synonyms consists of two parts: there are on one hand the cells which elaborate the specific chemical substance, on the other, the cells which respond to the presence of this substance when it is brought to them. The object of this letter is to point out that evidence exists that some at least of these linkages have been established by the evolution of a tissue responsive to a substance already produced within the organism for some other purpose or through some vagary of metabolism.

There are several examples of the apparently useless presence in relatively primitive organisms of chemical substances which in higher groups have acquired a physiological function as hormones. That adrenaline is present in certain annelids¹ is much more certain than that it has any endocrine function in this phylum. The specific substance of the mammalian posterior pituitary which causes contraction of the uterine musculature is represented even in the elasmobranch,² though it must be admitted that it is by no means certain that this substance has acquired a natural physiological function even in the mammal, and it is of course possible that it has some unknown function in the fish. A better example, therefore, is the presence of an oestrin in insects,³ since the occurrence of sharply-delimited gynandromorphism makes it highly improbable that there are functional sex hormones in this class. A converse case is the vestigial survival in the pituitary of the mammal, despite the disappearance of the responsive tissue, of the substance which causes the expansion of amphibian melanophores and teleost erythrocytes.⁴ Moreover, there are many examples of the extension of responsive tissue in evolution; thus the ventricular muscle of the mammal has developed a sensitiveness to adrenaline which is absent in the reptile.⁵ Is it too fanciful to regard the refractoriness of the genital organs of very young female rodents to stimulating hormones,⁶ or of the beating heart of the two-day-old chick embryo to adrenaline and acetyl-choline,⁷ as instances of phylogenetic recapitulation?

The most striking illustration for the present argument, however, is the demonstration⁸ of a substance in the anterior pituitary which stimulates the development of the mammary glands in the guinea-pig and of the crop gland in the pigeon, two analogous but by no means homologous organs, which must have developed separately their responsiveness to this (apparently) single substance.

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