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BEHAVIOR SYNTHESIS

THROUGH PIGMENT GENE PLEIOTROPY

CLYDE E. KEELER

Director Research Department, Central State Hospital
Milledgeville, Georgia

Formerly: Instructor in Ophthalmic Research, Harvard Medical School;
Research Fellow, Wistar Institute; Guggenheim Fellow.

REPRINTS and ESSAYS

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INTRODUCTION

Much of my early genetic research dealt with variations of the nervous system, the first of it having to do with rodless retina (retinal degeneration) and absent Corpus Callosum, both of the house mouse. For many years, however, I have oriented my studies toward a development of the concept that the unit of behavior tendency is the gene, although behavior involves much more than sense organs and a central nervous mechanism.

These studies demonstrate not only that the gene is the unit of behavior tendency, but they also provide a method for taming any wild species of bird or mammal due to the additive nature of pleiotropic modifications of glands, sense organs, brain and bodily form that accompany certain hereditary pigment variations. One must raise the wild species in great numbers and study the pleiotropic effects which accompany the pigment mutations that crop out. To produce a genetically tame strain then becomes merely a matter of adding together in the same individuals a number of pigment variations each known to be accompanied by a slight pleiotropically induced tamness tendency.

When I began this work the idea that behavior tendencies and patterns could sometimes be dependent upon a single gene was unthinkable to many, because they wanted to believe that behavior is something floating mysteriously above or over the matter of the brain but almost unrelated to its morphological details. Something not subject to the laws that govern the physical body, but rather something unique and independent with laws of its own. This attitude is probably a hangover of the theological or philosophical approach.

Indeed, one of my psychological colleagues was so convinced of this latter point of view that he went to higher authority, and there quietly tried to prevent my publication of a paper espousing the gene controlled nature of behavior trends, lest the announcement of such a relationship would be disastrous for the name of the college in which we both were teaching. Nor could I obtain publication of my first work in a popular science journal, because the editor was a psychologist who did not care to sponsor such a heresy. However, times have changed.

It is well known that gross behavior pattern alterations (commonly considered as abnormalities of behavior) are sometimes inherited as unit-characters in mammals (waltzers, jerkers, back flippers, circlers, shakers, etc. in mice; tumblers in pigeons; waltzers and shakers in guinepigs; Huntington's chorea, Oppenheim's disease, Friedreich's ataxia, spastic paralysis, progressive muscular atrophy, muscular distrophy, Thomsen's disease, syringomyelia, paroxysmal paralysis, Leber's disease, von Recklinghausen's and many other diseases in man.

The behavior anomalies of these syndromes are due to faulty morphological developments or degenerations that are reflected in physiological anomalies which, in turn, evoke abnormal behavior.

Because we also recognize many bizarre unit-gene-controlled behavior patterns resulting from alterations in several bodily systems simultaneously, it is not surprising that some trees of altered reaction, stemming from single genes, affect hair color in addition to other morphological characteristics at the same time. Some definitely abnormal behavior patterns may be recognized as associated with hair color and changes of form such as sensory defects in the homozygous blue merle collie, deafness in the blue-eyed-white English bull terrier and the white cat, epileptoid fits in the Vienna White rabbit, abnormal movements in Varitint Waddler mice, mentally retarded behavior in Følling's disease and the Chediak-Higashi syndrome in man.

Having studied trees of pleiotropic modification in morphology, physiology and behavior within the normal range associated with a number of coat colors, we ought to be able to purposefully combine several trees of altered reaction to produce more extreme reaction tendencies (since their presence is always indicated by a particular coat color), merely by inserting genetically into the same individual the several simply inherited coat color genes.

Among Norway rats and mink some individuals bearing mutant coat characters exhibit a wilding tendency (curly in rats, Kohi-nur, Blufrost, Baldy in mink) whereas individuals bearing other coat characters exhibit a taming tendency (cinnamon, black, hooded, pink-eyed dilute in rats; pastel, silverblu, albino and black-eyed-white in mink).

It is not surprising to find in Norway rats that the laboratory albino (containing black, hooded, and albino genes) is much tamer by nature than animals containing the black, hooded or albino genes singly, since the reductions (olfactory bulbs, adrenals and gonads) produced by these genes singly, become somewhat additive when the three genes are combined in the constitution of the laboratory albino rat.

It is quite understandable that the wilding tendency of the blufrost gene appears to be reduced by the taming of the silverblu gene when the two genes are combined homozygously in the same individual mink.

We have indications that such alterations, within the normal range of behavior for the species, are found in many animals including horses, cattle, dogs, foxes, squirrels, raccoon, Peromyscus, rabbits and man, as well as in the cases alluded to above in mink, rats and mice. By employing these animals it should be possible to synthesize behavior trends within the normal range, as has been done with the laboratory albino rat.

This principle applies to the schizophrenic Red fox with his anxiety complex over "what might happen" and his fear of "everything that does".

This principle provides a method of producing tame strains from feral species, a problem that baffled Darwin, because he did not recognize pigment gene pleiotropy.

If all this is true for mammals, it probably applies to such pigment variations in man as albinism and red hair with medically important consequences.

Thus, my mammalian studies especially of rats, mink and foxes lead up to the question of pigment gene pleiotropy in man with interesting and useful findings.

Although the researches on man have been carried out simultaneously with those on the infrahuman mammals, for the sake of order I have presented them in the sequence of rats, mink, foxes and man.

It is axiomatic that the style of scientific contributions shall be dry, statistical and uninteresting except for the graphs and numerical tables of bare facts wrested from the experiments and their implications for further research and application. However, this is not to say that scientist experiences no interesting moments or situations in the pursuit of his facts. In order to recount how some of these researches came about, I have inserted short essays describing a few situations which do not lend themselves to the approved formula of the "scientific article". For this may the gods of science forgive me.

Financial support for these researches has come from the Rockefeller Foundation and the Southern Fellowships Fund, as well as NIH and NIMH grants that are credited specifically in the articles reprinted here.

1

HOW IT BEGAN

"Do you hear that rat squealing?" asked Miss Meeser as she paused before the sensitive balances upon which she was weighing a pair of most carefully dissected rat adrenals to tenths of milligrams.

"Yes, I hear it, but what about it?" was my casual reply.

"It's a black one," said Miss Meeser.

"A black one? Do you mean to tell me that the voices of black rats are different from those of other rats? You'll have to show me."

We went through the open door of the Colony Office and down the hall to the source of the controversial sounds. There we found two black mutant Norway rats fighting.

I was impressed. "Can you distinguish any other colors of mutant rats by their voices?"

"Well I can distinguish the mutant albinos", said Miss Meeser, "their voices sound like a silver flute".

At this I began to wonder if Miss Meeser hadn't talked me into the idea after all that the voices of black rats were distinctive and that now she was trying to convince me of something even more preposterous. "Is Miss Meeser slipping mentally?" flashed through my mind.

"When you hear the silver flute please tell me".

Several weeks passed and then one day Miss Meeser said, "There it is!"

"What is?"

"The silver flute!"

I had heard it, too. It did not sound to me quite like a silver flute, but it was a whistle tone very unlike the raucous voice of a gray Norway rat. We traversed the hall, and there Miss Meeser pointed in triumph to a cage where two mutant albinos were fighting.

"You win. Do you know any more unique traits associated with coat colors in rats?"

"Yes, black mutants are tame by nature, and there are some other traits".

I went to lunch and on the way I met my friend, Dr. Radcliffe, Pathologist for the Philadelphia Zoo. I told him about the rat voices. He listened with a smile and then, while tapping his head ominously, he advised me not to publicize this matter too much until I had recorded these voices in some fashion that would not involve the judgement of the investigator.

At the Moore School of Electrical Engineering I found a sound analyzer first built to show how a Strandevarius differs from a cheap violin. Once a prima donna had been induced to vocalize into the microphone, but aside from that the machine had gathered dust for fifteen years. Ralph Showers brushed off the apparatus, corrected the "bugs" and we started recording adult male voices of rats having different coat color mutations, each voice sample elicited by a sharp pinch of tongs on the tail. The results showed the voices of blacks differ from wild grays by four keys on the piano. The mutant albinos had a voice consisting of a high pitched single frequency, and a single frequency is a whistle tone!

One day Miss Meeser said to me as I came into the laboratory, "Just feel the muscles of those rat carcasses that I have to dissect".

I could think of more pleasant pastimes than manually testing the tonus of body muscles of dead rats. However, I obliged and was astounded to find gray Norways to be very solidly constructed, certain mutants somewhat limp, and the Wistar albinos the flabbiest of all.

"So even muscle tonus can be changed by a single coat color gene mutation."

I made a cross between gray Norway and Wistar albino just to observe the hereditary transmission of some of the traits Miss Meeser had been talking about. The second generation had grown up without handling and several dozen of them occupied a large cage in one of the rooms until a caretaker reported cockroaches in that particular cage. We had to transfer the rats at once to another cage so that the old cage could be sterilized.

Miss Meeser said, "You have been used to mice at Harvard, so you'd better let me handle this situation".

She put on her heavy pigskin gloves and with stout obstetrical forceps withdrew the vicious, shrieking, thrashing, jumping, urinating, defecating monsters by their tails one by one. When she had transferred all but three or four she removed the gloves, laid down the forceps and lifted out a quiet, unperturbed rat on the palm of her hand.

"How did you dare do that?" I gasped.

"It was a black one", said Miss Meeser, "and you noticed that it made no attempt to bite".

From that moment on the principles of pigment gene pleiotropy, with their effects on morphology, physiology and psychosomatic behavior became the principal objects of my research.

Miss Meeser had been Dr. H.H. Donaldson's laboratory assistant and every working day for seventeen years she had dissected for him ten adult rats of a given age, five males and five females. She had weighed various organs meticulously, and entered the results on library cards.

Dr. Donaldson wanted these data for his fruitless study of the inheritance of acquired characters. He died in his eighties without being able to make use of his voluminous data because they could not solve his problem.

When I went to the Wistar Institute following Dr. Donaldson's death, I was given his thousands of records. I had them on my shelf for one and a half years without finding a use for them. After Miss Meeser had initiated me into the new world of mutant coat color genes in rats and the idiosyncracies that they produced I suddenly saw the light.

Dr. Donaldson's dissection records would explain the physical modifications of glands, sense organs and brain that bring about unique changes in physiology that in turn determine alterations in behavior.

So for a number of months I studied these records, and they corroborated my theory.

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MULTIPLE EFFECTS OF COAT COLOR GENES IN THE NORWAY RAT, WITH SPECIAL REFERENCE TO TEMPERAMENT AND DOMESTICATION[1]

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The Wistar Institute, Philadelphia

Received March 11, 1942

INTRODUCTION

Ever since Darwin's epoch-making studies it has been widely held that domestic animals bear in their grossly modified morphology and behavior the indelible stamp of their captivity; that these domesticative changes began as almost imperceptible alterations and were increased through many generations of painstaking selection by primitive man.

This hypothesis was embraced by environmentalists and geneticists alike because the former perceived in the phenomenon of domestication the pressure of the milieu molding the plastic characters and germplasm of organisms, and the latter saw in it a selection of small-effect gene mutations occuring spontaneously within the germplasm. Neutrals recognized in the theory an opportunity for both extremes to be partly right, in that the environment could induce a host of small-effect germinal mutations by the Lamarckian method, and these could be selected by the environment in the Darwinian sense. Orthogeneticists noted the same kinds of modifications in so many domestic mammals that it appeared to them as though a teleological purpose or destiny had stretched out its mystical hand and was drawing domesticative evolution toward a clearly defined goal.

Everybody was happy, each scholar recognizing the undeniable facts of modification, and each interpreting them in the fashion that pleased himself most, without anybody being able to severely criticize another's views because of the great difficulties involved in attempting to put the matter to an experimental test.

Not only were the factors of cost, time and space prohibitive, but in addition, there was no agreement as to a suitable mammal for the experiment.

In this state of impasse the problem was shelved and largely forgotten.

MATERIALS AND METHODS

The late Dr. Henry H. Donaldson of the Wistar Institute spent much time comparing the morphological characters of tame albino rats with those of wild gray Norway rats, from which type the albino must have been derived.

The differences found were similar to those reported by Darwin ('83) for domestic rabbits and caused Dr. Donaldson to state in 1915:

[1] Paper presented on the program of the American Society of Zoologists, Dallas, Texas, with minor amplifications.

> When the body lengths are the same: The Norway rat has a smaller body weight, a greater brain weight; a greater spinal cord weight, a higher percentage of water in the central nervous system; heavier testes, ovaries and suprarenals. . . .
>
> These differences taken together indicate that the albino rat has grown less well, and it seems most natural to attribute this lack of growth to the whole set of conditions summed up in the word "domestication."

Obviously, there were two morphological methods of approach to this problem.

First, tame albinos could be turned loose in appropriate isolated habitats in which no Norway rats lived, after which, samples of the population could be measured from time to time to see if feralization of the albino would cause it to reassume the anatomical and behavioristic characters of the Norway.

Second, gray Norway rats could be caught in the wild, and maintained under conditions of domestication. Periodic measurements taken on this population would reveal any trend toward bodily form and behavior of tame laboratory albinos.

Dr. Donaldson's point of view was Darwinian, Lamarckian and at times even orthogenetic, and hence he neglected the direct genetic approach in favor of the morphological. He attempted on four separate occasions (Donaldson '16) to feralize tame albino rats but without success.

In 1919 Dr. King undertook a comprehensive study of the effects of domestication on the wild gray Norway rat; a long range program that has many aspects still under investigation.

At Dr. King's suggestion, Dr. Donaldson followed these captive gray Norway rats for thirty-five generations, but was unable to find the changes that he believed that domestication should have conferred upon them (King and Donaldson '29).

When in 1927 mutant albinos appeared in Dr. King's captive gray strain, she observed that they bore slight morphological differences as compared with the gray Norways from which they were derived.

Some of the modifications were in the direction of the tame laboratory albinos previously observed, and Dr. King expanded her domestication program to include mutant albinos in two colonies, one maintained at the Wistar Institute and one at the Morris Biological Farm.

Dr. Donaldson followed these two mutant albino captivity experiments through eight generations (Donaldson, unpublished data) but the mutant albinos remained essentially wild gray Norway rats save for color and the morphological deviations noted in the original mutants.

Dr. Donaldson died in 1938 leaving the problem of modification in domestic mammals unsolved, but it is possible from the more than 2000 meticulous dissection records that he left to attack the problem once more, in the light of newly gathered information on the important behavior side, and from a viewpoint that is genetic.

INDIVIDUAL GENES DISPLAYED UPON A UNIFORM, RESIDUAL HEREDITARY BACKGROUND

Scientists have never been able to study adequately the modifications of bodily form and behavior of mammals due to individual genes, because of the hetero-

geneity of myriads of gene allels composing the residual hereditary backgrounds of various stocks observed, upon which backgrounds the effects of individual genes are frequently distorted or obscured.

But Dr. King's captive gray Norway rats have a uniform, somewhat inbred, residual hereditary background upon which to display, recognize, and compare the morphological and behavioristic effects of any visible mutations that may arise in this stock.

And a veritable epidemic of mutations (King '32), most of them expressed in coat-colors, did occur in the gray Norway strain from which were derived mutant sub-strains of piebald, ruby-eyed dilute, black, curly, albino, albino-waltzer, cinnamon and stub.

Dissections were made of animals bearing each of these mutations in addition to records of various organ weights. From Dr. Donaldson's point of view, the slight modifications that were found in the mutants were merely indications of a general weakening of the developmental process produced by mutations of any sort.

But from the genetic point of view, the effects observed may be considered largely the results of the coat-color genes marking the sub-strains, because of the common residual hereditary background upon which are displayed the effects of each mutant gene.

TRENDS OF BEHAVIOR IN MUTANT STRAINS

When the various mutant genes are displayed upon this common residual hereditary background, it is found that animals bearing these mutations exhibit entirely different personalities than observed in captive gray Norway rats, personalities that have characterized the several mutant strains ever since their origin.

The following character sketches are derived from independent descriptions by 5 observers working with these strains over long periods of time.

Mutant albino. Cringe when approached after being completely tamed. When tamed, about as apt as the tamed grays to bite or fight back when picked up. When not tamed, as wild and vicious as the grays. When dropped on the floor they attack the caretakers as grays may do. Voice[2] may be a high, sustained whistle with fundamental tone at a frequency of 2800 cycles per second and having no overtones, whereas the rough, loud gray Norway voice may have a fundamental at 400 with overtones at 2200 and 4400.

Ruby-eyed dilute. Known to be fairly sluggish, but not now available for study on the original background. Voice, a high sustained tone with a frequency of 2200.

Cinnamon (Brown pigment). Easier to tame than grays, but may revert to wild nature after being tamed. Vigorous and active. Ordinarily more peaceful than grays, but when called upon to fight they fight quite as well as grays. Rough, loud voice similar to that of the gray Norway with fundamental frequency at 400.

[2] Oscillograph records made in collaboration with Mr. Ralph M. Showers, The Moore School of Electrical Engineering.

Curly. Even after being tamed difficult to catch, but when removed from the cage and held in the hand, they ordinarily do not bite. They never can be entirely trusted. Voice: low, unsustained, with many varying components. The fundamental frequency is about 500.

Black. Sluggish. Already tame by nature. If very excited they may click their teeth, but are not apt to bite. Many only whine softly when picked up with tongs. Voice may be a high, sustained tone with fundamental at 1100 or 2600.

Albino-waltzers. Easier to tame than mutant albinos from which they were derived, but always exceedingly nervous. When tamed, they seldom turn on the observer. Voice not tested.

Stub. Dwarfed, frequently tailless. Always fighting each other. Go out of their way to pick trouble. Do not mind their own business as do gray rats, but throw their bodies against the cage wire when anyone approaches. Voice is a high squeak with great amplitude at high frequencies. The fundamental is at 1100. Both 2200 and 4400 predominate with the peak at 6600.

Piebald. As wild as gray. Not now available on the original gray background. Voice not tested.

Voice box shapes were examined and it was found that size and shape of voice box may be correlated with quality of voice.

Dr. King has collected complete growth, fertility and longevity records on several of these mutant strains that will be of great interest for a study of the physiological effects of the coat-color genes involved.

MODIFICATION PROFILES

If a list of anatomical and behavioristic characters is prepared for each strain, and these average values are thrown into percentages as compared with the gray Norway, we can represent graphically all deviations for a mutant strain in a modification profile (fig. 1). The modification profiles of several mutant strains may be compared. Modification profiles will vary with sex and also with the individuality of the mutation under observation. In the charts, black areas represent data for males, dotted lines those for females.

Data upon more than 1472 animals are represented in our charts.

The numbers of individuals upon which the morphological data depend are adequate for statistical purposes, save for black mutants. For example, the gray Norway stock, measured at about 600 days of age, includes 304 males and 304 females. The other stocks represented in our charts include mutant albino: 211 males, 206 females; brown (cinnamon): 60 males, 69 females; piebald: 17 males, 19 females; curly: 76 males, 84 females; black-piebald: 42 males, 47 females; albino-waltzer: 16 males, 17 females.

Although inferiority of brain weight is not indicated in figure 1 for mutant albino males and brown males, final data show that brain weights of each mutant type are inferior to brain weights of gray Norways by amounts which, when the

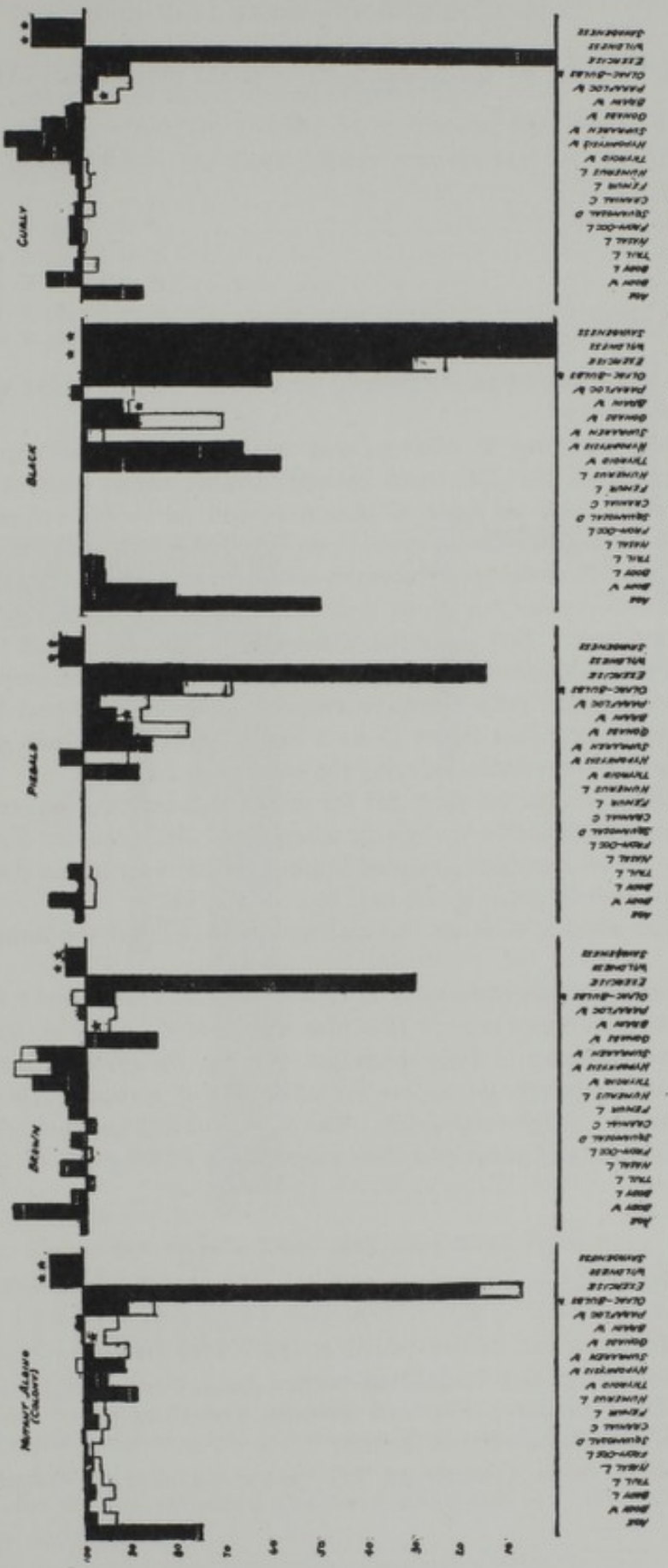


FIG. 1. MODIFICATION PROFILES FOR THE MUTANT STRAINS: ALBINO, BROWN, PIEBALD, BLACK AND CURLY

Average values for each character in a mutant strain are represented relative to the average gray Norway value for that character taken as 100 per cent.

differences are divided by the probable errors of the differences yield quotients, as follows:

	$\frac{\text{Diff (Gray Norway-Mutant)}}{\text{P.E. Diff}}$
Mutant albino	♂ = 17.74; ♀ = 27.72
Brown (cinnamon)	♂ = 5.38; ♀ = 3.02
Piebald	♂ = 62.27; ♀ = 30.96
Curly	♂ = 11.59; ♀ = 18.44
Black-piebald	♂ = 87.14; ♀ = 107.46
Albino-waltzer	♂ = 9.06; ♀ = 19.03

Values for other important characters, such as for various gland weights, are statistically significant.

Although our measures of wildness and tameness are of the impressionistic sort, we believe that the differences between strains are so distinct that their validity is certain, and we hope to obtain refined numerical values for these behavior traits in the near future based upon psychological tests.

Our measurements of voluntary exercise are based on "wheel records." These records are admittedly few, and individual variation exists in each strain between sexes and individuals. But the strain differences are so great that the general conclusions drawn from the wheel records corroborate the general impressions of activity. For example, gray Norways averaged between 3000 and 5000 wheel revolutions per twenty-four hours (3 to 5 miles), whereas mutant albinos ran between 100 and 700 revolutions during the same period of time.

If modification profiles are prepared for stocks bearing two coat-color genes, there are found cummulative changes in morphology and behavior (fig. 2).

Thus, if we study a certain strain of black-piebalds, we can see the effects of both black and piebald genes in the modification profile.

Other bigenic stocks, such as the waltzer-albino, exhibit the same phenomenon.

From the foregoing observations it is evident that coat-color genes modify detailed morphology in many ways. It is also clear that the basis of temperament and behavior is inherited in gene controlled patterns, the effects of a single gene being distributed irregularly throughout the whole field of response, like dabs of a particular color in a polychrome print. The complete basic-response picture is the sum-total of the effects of genes and their interactions in all parts of the field of response.

DOMESTICATION OF THE TAME ALBINO RAT

But how can we apply these findings to the problem of domestication of the tame albino rat?

Dr. Shinkishi Hatai had demonstrated at the Wistar Institute that the tame albino rats studied by Dr. Donaldson carried both black and piebald genes latently, but Dr. Donaldson dismissed the idea that these genes could be important factors in domesticative evolution.

Thus, in 1924 he wrote, (Donaldson '24) "as yet we have no evidence for any

correlation of the somatic characters so far as studied, with those *slight differences in gametic composition* of the common albino strain . . . ."

But from the modification profiles it is learned that some of the supposed domesticative changes in the tame albino rats studied by Dr. Donaldson, must

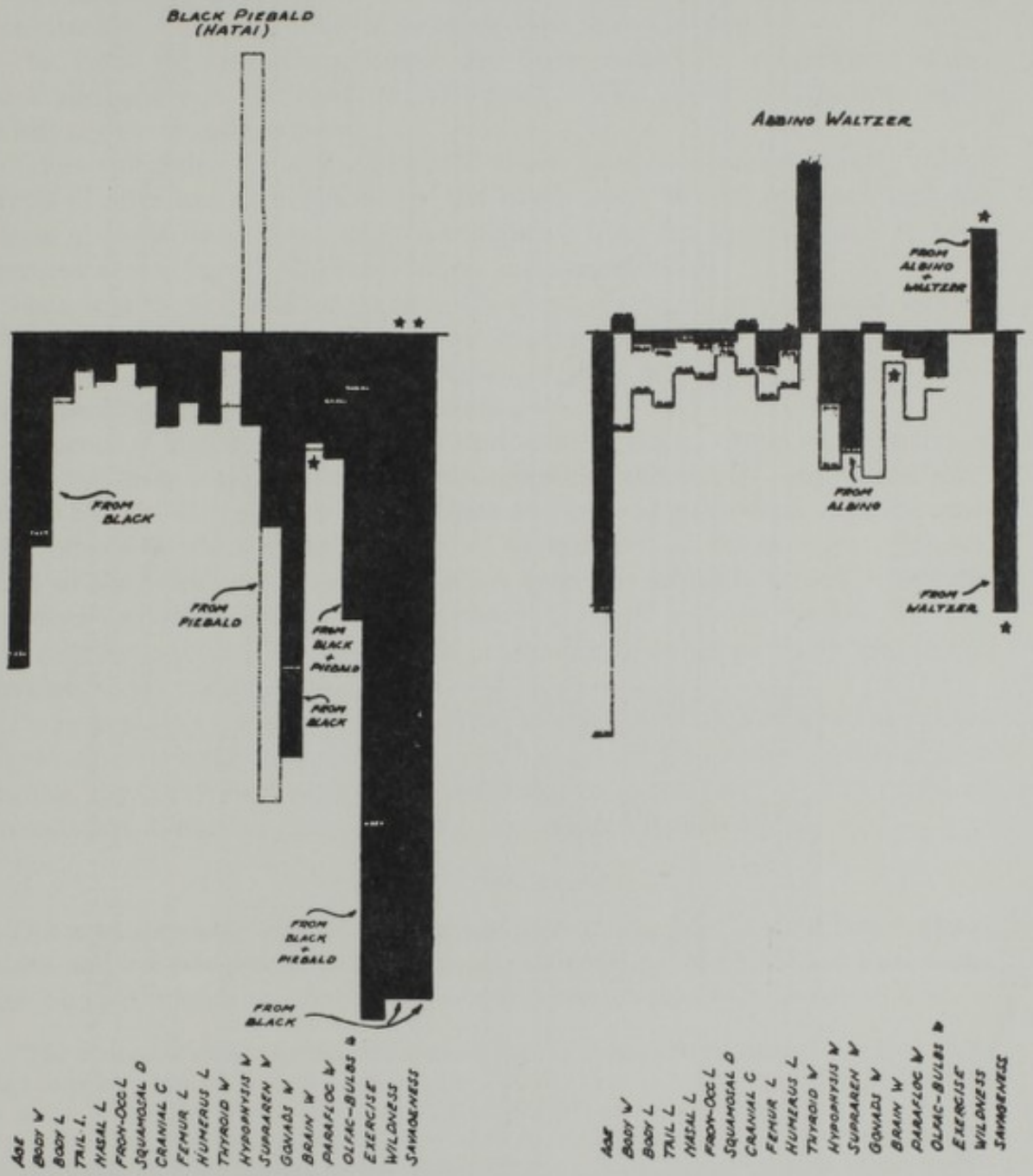


FIG. 2. MODIFICATION PROFILES FOR TWO BIGENIC STOCKS: BLACK-PIEBALD AND ALBINO-WALTZER

The possible gene-origin of various alterations is suggested by arrows

have been due to the combined effects of the genes for black and piebald, upon morphology and behavior.

When the measured characters are arranged vertically upon a chart (fig. 3),

FIG. 3. DIAGRAM TO SHOW THE EFFECT OF THE THREE GENES: ALBINO, BLACK AND PIEBALD IN ACCOUNTING FOR "DOMESTICATIVE MODIFICATIONS" IN THE STRAIN OF TAME ALBINO RATS STUDIED BY DR. DONALDSON

Degrees of modification are represented in per cent, the average value for each character in the gray Norway being taken as 100 per cent and the average value for each character in the albino being taken as 0 per cent.

and the 100 per cent line is considered to represent the values of the listed characters for the gray Norway, the 0 per cent line may represent the corresponding values for the tame albinos, that is, the final stage of evolution for each character.

The distance between the two vertical lines measures for each character the modifications commonly believed to result from domestication.

The value for each characteristic has been plotted for the mutant albino stock and added to the chart in solid black. This shows modifications made principally by the albino gene.

Values calculated for a black-piebald strain have been added directly to the effects of albinism, as indicated by the ruled area. It will be noted that the effects of these three genes carry modification from the gray Norway in most characters even beyond the tame albino goal (unshaded).[3]

Thus, it seems probable that the tame albino rat, at least the strain studied, was not domesticated by painstaking selection over long periods of time, but was modified in morphology principally by the introduction of three coat color genes, and in behavior particularly by the (non-agouti) black gene.

A survey of eighteen stocks shows that most of the naturally tame strains of albino rats now employed in American scientific laboratories were tamed principally by the black gene or by the black and piebald genes combined, the coat-color effects of which genes are masked by albinism as we have stated above. Most of the stocks not bearing the black gene are probably tamed principally by other mendelian genes such as pink-eyed yellow, red-eyed yellow, hairless, and ruby-eyed dilute, because strains containing these genes singly are, in our experience, invariably tame.

There is some evidence to indicate that mendelian coat-color genes may have played an even more important role than has man in the domestication of farm animals, by providing attractive coat-color correlates for certain preferred domesticative behavior complexes that man desired to select.

HUMAN APPLICATIONS

The most important contribution of the present study is its proof that temperament and behavior are inherited in gene controlled parcels and that personality may be synthesized by combining various behavior-modifying genes.

[3] The method of obtaining the values which appear in figure 3 is illustrated by the following example. Assume that the typical gray Norway female weighs 300 grams at 600 days of age and that the Wistar Albino female weighs 200 grams at the same age. Then 100 grams decrease in weight equals 100 percent of the supposed evolutionary change in body weight from the gray Norway to the Wistar Albino. If the female mutant Albino has an average body weight of 260 grams, this represents an evolutionary change toward the Wistar Albino of 40 grams or 40 percent. But the Wistar Albino also contains in addition to the albino gene the genes for black and piebald. By examining the data for a black-piebald strain segregated from an outcross to gray Norway rats, it is found that the average weight for black-piebald females is 210 grams. This weight represents an evolutionary change toward the Wistar Albino of 90 grams or 90 percent. By adding the percentage reduction in body weight for the mutant albino and black-piebald strains, 130 percent is obtained, or 30 percent beyond that which is expected.

This excess is undoubtedly due, in a measure, to the fact that addition is actually not at face value but frequently at a discount. The details of such cumulative gene interactions with their bonuses and deductions cannot be predicted in advance.

The implications are in line with certain data in the fields of psychiatry and psychology which tend to indicate that this mechanism applies also to man, and our demonstration in the case of the Norway rat seems to necessitate a consideration of hereditary factors in all future experiments dealing with behavior.

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III

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THE ASSOCIATION OF THE BLACK (non-agouti) GENE WITH BEHAVIOR

In the Norway Rat

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IN a paper presented before the American Society of Zoologists in Dallas December 1941 there was given a general account of what were interpreted as the pleiotropic effects of certain coat-character genes upon morphology and behavior.[1]

In that preliminary report evidence was presented to show that in certain crosses of the Norway rat there was a definite association between coat color genes and temperament. These crosses were between albino rats of the Wistar strain, which carry black, and wild gray Norway rats. In the coat color segregates in F_2 and later generations it was found that the rats carrying the black gene tended to be tamer and less aggressive than the gray segregates. The observations there reported have been supplemented and new tests have been applied to assay the temperamental differences, so that the findings are now based on a large enough body of data to have unquestionable statistical significance.

The question of whether these temperamental differences are due to the pleiotropic effects of the actual coat color gene, or to the close linkage of that gene with distinct temperament genes is not completely settled by the data here presented. The writer is inclined to believe that pleiotropy rather than linkage accounts for these effects. Evidence favoring pleiotropy of the taming effect associated with the black (non-agouti) gene rather than linked-genes is as follows:

1. Of the tame laboratory strains of Norway rats in America, it was learned mainly by correspondence that the following contain the black gene: August 990 (by mutation), Fischer 6, Fischer 230, Fischer 344, King Inbred, Marshall 520, McCollum, New Haven, Osborne-Mendel, Philadelphia, Riddle, Curtis-Dunning selfed 34069, Sherman, Sprague-Dawley, Wistar Albino, Wistar Piebald, Yale, Zimmerman 61. Although these strains (except August 990) may possibly trace their black genes to the same mutation a hundred or more years ago, because most laboratory strains are distantly related, still these strains must have provided in recent years a great variety of residual hereditary backgrounds upon which to display the probable behavior tendencies of the black gene. Some of the strains named above have independent origins. Some are descended from Wistar Albinos; some from the Osborne-Mendel group. But because both of these source strains had mixed origins, it appears that some opportunity has been given originally for separating the black gene from any possible linked taming gene. The same applies to the August 990 strain during its origin. An additional black strain is said by Dunning to be wild, but whether the wildness here is due to linked genes or to other genetic changes cannot be determined except by a long breeding program.

2. A survey of stocks at the Wistar Institute revealed the fact that two black strains were derived by King from outcrosses of tame albino (carrying black) to wild gray Norway. These black strains were tame. Another strain of tame blacks was derived from a mixture of segregates from several outcrosses of different strains containing black. It is known that Hatai (1914) made an outcross of tame Wistar Albinos (carrying black) to wild gray Norway rats. From this cross there descended a self black and a black hooded strain. The black hooded strain exists today, and is tame.

The black strain is extinct, but is reported verbally by members of the Wistar staff to have been tame.

The Lashley and the Long-Evans strains arose from similar outcrosses of tame albinos carrying black, to gray Norway. Castle (personal communication) has examined a pair of black rats from the Long-Evans strain and reports them "well behaved." Enders (personal communication) finds his black hooded derivatives of Lashley's cross to be tame.

Each of the above named crosses gave opportunities for crossing-over between the black gene and possible, linked, tameness genes if such had been present.

3. Because King's mutant black stock was derived from the recessive black individuals that segregated from her gray Norways during at least four consecutive generations, there were many opportunities in five or more generations for crossovers between the recessive black gene in heterozygous state and any possible linked taming gene or genes. Today, tame black mutants are segregating from the 56th generation of gray Norways. One adult black segregate has been examined and found to be tame as compared with its gray siblings. If this is a continued segregation of the old black mutation, rather than of a new mutation to black, there have been manifold opportunities for crossing over in at least 44 generations on the linked gene assumption. If a new mutation, there must be assumed the simultaneous mutation of at least one linked tameness gene, unless we accept the pleiotropy hypothesis. At least 25 of the earlier black segregates from the King gray strain have come under the observation of several persons, who describe them all as tame by nature. No black mutants were observed to be wild.

4. King has a strain of chocolate rats derived from Cinnamon plus black (non-agouti). They are tame. Castle has made crosses with some of these animals and states (personal communication) that chocolate segregates are in general tame, whereas cinnamons may be wild. Hence it would appear that the taming effect associated with the black gene in duplex can overcome the wilding effects not only of the gray Norway background, but also of the gray Norway background plus the cinnamon gene in duplex.

The present paper also bears out the foregoing lines of evidence, in that marked behavior differences appear between black (non-agouti) and gray Norway rats segregating from a cross of wild gray Norway to tame Wistar albinos.* This study, unlike the earlier one based on impressionistic observations[1] utilizes certain simple behavior tests for the purpose of recording individual responses to definite situations. Such responses could be subjected to mathematical checks for the statistical significance of such differences in behavior as might be correlated with black and gray coat colors respectively.

Materials

Three Wistar albino females were mated to a gray Norway male, and hence it may be assumed that in the hybrids to be described, we are always dealing with the same identical black gene.

Wistar albinos are homozygous for the three independent Mendelian recessive coat-character genes: albino, hooded (piebald) and black. Because these genes are all recessive (hooded giving in simplex a white belly spot, white paws and white tail tip) nothing except grays hybrid for all three recessive genes are obtained in the first hybrid generation. When a second hybrid generation is produced by crossing together members of the first hybrid generation a normal, trihybrid, mendelian ratio is obtained of theoretically 27 grays, 9 albinos, 9 hooded, 9 black, 3 albino hooded, 3 albino-black, 3 black hooded, and 1 albino-black-hooded. In such a segregation there will be homozygous grays and grays ranging from those hybrid for any one up to all possible combinations

*Blacks and grays were chosen for intensive study because these two color-groups gave the most clear-cut distinctions of any of the color-groups reported upon previously by Keeler and King.[1]

of the three recessive characters. Albinos may carry one gene or two genes for any or all of the possible combinations of coat characters or they may carry none of them. The blacks, on the contrary, cannot carry the gene for gray, although they may carry a gene for albinism without detection.

Thus, albinos will be useless for comparisons, and grays will be expected to be more variable than blacks in behavior.

One hundred and twenty-five F_2 and backcross segregates (heterogeneous as to color), derived from the cross described above, were available. These have been subjected individually to several tests such as those listed by Hall.[2] The results of these tests may be compared by color classes.

The test segregates have been raised with animals of the several color varieties confined in the same cages. It is now realized, however, that there are possible advantages in raising each coat-color class separately for the purpose of revealing all the inborn behavior differences existing between color classes, because of the probable environmental influence of cage associates upon behavior of the individual.

It may also be mentioned that sexes were separated, and about the same number of rats were kept in each cage because of the taming effect of crowding and the wilding effect of few associates or solitude. The average number of rats to a Wistar cage was five. Segregates were not handled from the time of weaning on, nor were they allowed to become previously familiar with the observer, in order that maximum differences could be obtained in the adults.

We might expect the first test on segregates to be the most significant, because even wild rats become tamer with handling and soon are accustomed to a particular observer, as is evidenced by the holding experiments about to be described. Indeed, they probably become tame and docile in the hands of a particular observer long before they may be handled by others.

It may be stated that the hybrid rats of this series had become accustomed to the presence of persons in the laboratory although they had not been handled. As a group, they gnawed their cages very much, as do wild grays and mutant albinos, in contrast to all other strains in the laboratory. This fact is an indication of their greater average activity.

First Holding Test

For the first holding test the door of each cage was opened and a rat was

TABLE I. First Holding Test.*

Color of Segregates	Gray	Albino	Gray Hood	Gray + Gray Hood	Black	Black Hood	Black + Black Hood	Significance Gray vs Black
Number of Rats	45	28	22	67	23	7	30	
% Biting	34	28	45	40	13	0	10	hs
% Attacking	4	14	18	9	4	0	3	–
% Squealing	67	71	73	68	39	28	37	hs
% Opening Mouth	0	0	4	1	0	0	0	–
% Laying Ears Bkk	49	18	36	45	9	1	10	hs
% Puffing	7	17	18	10	0	0	0	–
% Whining	17	10	18	18	4	2	10	x
% Chittering	2	7	18	18	4	0	3	x
% Urinating	53	46	45	51	9	0	7	hs
% Defecating	73	75	64	70	43	57	47	s
% No Reaction	2	7	0	1	30	28	30	hs
Av. No. Reactions	3.11	2.75	3.41	3.22	1.26	1.28	1.27	

*The significance of differences in reaction between gray and gray hooded vs. black and black hooded rats recorded in the tables, has been determined through the kindness of Prof. H. M. Lufkin using Fisher's chi-square method. Chances less than .05 and greater than .01 (following Snedecor) are considered significant (marked *s*). Chances less than .01 are highly significant (marked *hs*) and those greater than .90 have no significance (marked *x*).

The method used for determining the significance of differences between the means for reactions consists of first setting up a fourfold table of coat color against frequences of reactions and non-reactions. The value of chi-square is obtained for one degree of freedom, and with Yates' correction applied. Fisher feels that this is more satisfactory than the use of the point-binomial. (See Fisher and Yates,[4] p. 3.)

taken at random in the observer's heavily gloved hand. As little commotion as possible was caused. The animal was withdrawn from the cage and held quietly in the hand for one minute during which time a number of possible reactions were counted that are recorded in Table I.

For purposes of comparison the albinos are of little value, because we do not know which individuals carry and which do not carry black latently, as mentioned above. Because we are really desirous of comparing merely the differences between animals bearing two doses of the black gene and ones bearing its gray allel homozygously or heterozygously, we have combined grays with gray hoodeds and blacks with black hoodeds. Here we find the grays have a higher score than the blacks for biting (40:10%), attacking (9:3%), squealing (68:37%), opening mouth (1:0%), laying ears back (45:10%), puffing (10:0%), whining (18:10%), chittering (18:3%), urinating (51:7%), defecating (70:47%). One per cent of grays and gray hoodeds gave no reaction against 30% for blacks and black hoodeds. The average number of reactions per individual was 3.22 for grays and 1.27 for blacks. When these figures are examined statistically it is found that the differences in response for blacks and grays are highly significant for biting, squealing, laying ears back, urinating and no reaction. The difference is also significant for defecating.

The above described observations were made on February 16. An annoyance test was carried out by nose-tickling with brush bristles on March 2. Two emergence tests were conducted on March 3 and March 4 respectively. Then a second holding test was made on March 5. This time the blacks and black hoodeds were removed last from each cage, it being supposed that the commotion of removing the grays might change their recognized tame behavior. However, the differences between blacks and grays have not been eliminated entirely as will be seen in Table II.

TABLE II. Second Holding Test.

Color of Segregates	Albino	Gray	Grey Hood	Gray + Gray Hood	Black	Black Hood	Black + Black Hood	Significance Grey vs. Black
Number of Rats	28	45	22	67	23	7	30	
% Biting	7	20	18	19	9	0	7	x
% Attacking	0	11	0	7	4	0	3	x
% Squealing	18	55	27	46	35	28	30	x
% Opening Mouth	0	2	0	1	0	0	0	–
% Laying Ears Back	7	60	0	40	17	0	13	hs
% Puffing	3	9.	5	7	0	0	0	–
% Whining	14	9	0	6	9	71	23	x
% Chittering	0	4	5	4	0	28	7	x
% Urinating	32	47	32	42	30	14	27	x
% Defecating	50	47	27	40	69	43	63	s?
% No Reaction	11	4	9	6	9	14	10	x
Av. No. Reactions	1.32	2.64	1.14	2.15	1.74	1.86	1.77	

Second Holding Test

Grays and gray hoodeds combined still exceed blacks and black hoodeds in the second holding test as regards biting (19:7%), attacking (7:3%), squealing (46:30%), mouth opening (1:0%), laying back ears (40:13%), puffing (7:0%), and urinating (42:27%), and also in number of reactions per individual (2.15 : 1.77). The blacks plus black hoodeds exceed the grays plus gray hoodeds in whining (23:6%), chittering (7:4%), defecating (63:40%), and no reaction (10:6%).

From this table compared with Table I, it will be seen that familiarity with the experimentor and experimental conditions in grays plus gray hoodeds has probably reduced biting (40% to 19%), attacking (9% to 7%), squealing (68% to 46%), laying back ears (45% to 40%), puffing (10% to 7%), whining (18% to 6%), chittering (18% to 4%), urinating (51% to 42%), defecating (70% to 40%), and has increased no reaction (1% to 6%). The average number of reactions per individual is decreased from 3.22 to 2.15.

The excitement of being the last rats taken from the cage apparently has increased for blacks and black hoodeds

the number of reactions from 1.27 to 1.77. It has increased defecating from 47% to 63%, urinating from 7% to 27%, chittering from 3% to 7%, whining from 10% to 23%, laying back ears from 10% to 13%. In spite of this evidence of greater excitement in the blacks, attacking remained the same as formerly (3%), squealing decreased from 37% to 30% and biting was reduced from 10% to 7%. It will be noted that whining and chittering probably increased at the expense of squealing.

When these figures are examined statistically the differences between the responses of grays and blacks have been reduced so that those for biting, attacking, squealing, whining, chittering, urinating and no reaction have lost significance. Defecating has questionable significance. Laying ears back is highly significant.

First Emergence Test

In the first emergence test, designed merely to determine whether blacks emerged from the nest more quickly than grays, the door of a cage was opened and the voluntary emerging order of rats with regard to their coat colors was recorded for all the rats emerging during five minutes. The results are given in Table III. It will be seen for example, that 14% of the albinos achieved the distinction of being first emergent, 13% of the grays, 9% of the gray hoodeds, 30% of blacks, but none of the black hoodeds. Grays and gray hoodeds together scored 12% first emergents, while blacks and black hoodeds scored 23% of first emergents. Grays and gray hoodeds together scored 27% of first, second, and third emergents, as against 53% for blacks plus black hoodeds. If we consider the total of all emergence, grays and gray hoodeds have 36% emergents compared with the record for blacks and black hoodeds of 60% emergents.

But upon the basis of behavior uninfluenced by cagemates, first emergence should be given greater weight than second emergence, second emergence greater than third, etc. This is because after the first three rats have emerged without calamity, even very cautious rats may follow suite. If we weight the actual numbers of emergents (1st, 2nd, and 3rd) with factors of 3, 2, and 1 respectively and then divide by population size as we have done in Table III, we get a score of .55 for gray and gray hoodeds to be compared with 1.27 for black and black hoodeds.

TABLE III. First Emergence Test.

Coat Color	n	1st Emergent in %	2nd Emergent in %	3rd Emergent in %	1st 2nd + 3rd Emergents in %	4th Emergent in %	5th Emergent in %	6th Emergent in %	Total All 6 Emergents in %
Albino	28	14	14	7	36	7	0	0	43
Gray	45	13	4	13	31	4	4	2	42
Gray Hood	22	9	4	4	18	4	0	0	23
		12 ↑ X			27 ↑ S				36 ↑ S
Black	23	30	22	4	56	0	9	0	65
Black Hood	7	0	43	0	43	0	0	0	43
		↓ 23			↓ 53				↓ 60

Weighted Scores

	n	1st Emergent	2nd Emergent	3rd Emergent	Total Score
Gray + Gray Hood	67	(8x3) 24	(3x2) 6	(7x1) 7	67/37 .55
Black + Black Hood	30	(7x3) 21	(8x2) 16	(1x1) 1	38/30 1.27

When statistically examined, the difference in percentage for blacks and grays of individuals recorded as "first emergent" is not significant. But when first, second and third emergents are considered together, the difference between blacks and grays becomes significant. This difference is retained so that when all six emergents are considered together the diversity of response between gray and black is also significant.

Because this rough emergence survey indicated such distinct differences in behavior, it was decided to refine the test.

Refined Emergence Test

In the refined emergence test the door of each cage was opened in sequence and the time of emergence for each individual during three minutes was recorded by means of a stop watch. The results of the refined emergence test are recorded in Table IV.

It will be seen that of all animals emerging, grays and gray hoodeds averaged 84 seconds whereas the average time for blacks and black hoodeds to emerge was 57 seconds.

If the individual records are broken up into those emerging during the first, first-and-second, and first-second-and-third minutes respectively, 21% grays and gray hoodeds are found to have emerged during the first minute compared with 40% of the blacks and black hoodeds. During the first and second minutes, 40% of the grays and gray hoodeds emerged as compared with 63% of blacks and black hoodeds. During all three minutes a total of 49% of the grays and gray hoodeds emerged, whereas during this same time interval 73% of the blacks and black hoodeds emerged.

If one compares percentage of blacks emerging during the first minute with percentage of grays emerging during the first minute, the difference is not statistically significant. But if one compares blacks and grays emerging during both first and second minutes the difference is significant. When emergents of first, second and third minutes are compared, the behavior of blacks is significantly different from that of grays.

If one weights the emergents of the first minute with a factor of 3, emergents of the second minute with a factor of 2, and emergents of the third minute with a factor of 1, then the grays and gray hoodeds make a score of 1.10 to be compared with the black and black hoodeds score of 4.06.

Smoke-Blocked Emergence Test

Because it was noted that the gray rats were quickly becoming accustomed

TABLE IV. Refined Emergence Test.

Coat Color	n	Number Emerging	Total Seconds	Average Emergence Time in Seconds	% Emerging During 1st Minute	% Emerging During 2nd Minute	% Emerging During 1st + 2nd Minutes	% Emerging During 3rd Minute	% Emerging During 1st+2nd+3rd Minutes
Albino	28	15	805	54	36	18	53	0	53
Gray	45	21 (33)	1644	78 (84)	22 (21)	18	40 (40)	7	43 (49)
Gray Hood	22	12	1132	94	18	23	41	14	54
Black	23	16 (22)	918	57 (57)	35 (40)	26	61 (63)	9	69 (73)
Black Hood	7	6	336	48	57	14	71	14	86

Weighted Scores

	n	1st Emergent	2nd Emergent	3rd Emergent	Total Score
Gray + Gray Hood	67	(14×3) 42	(10×2) 20	(12×1) 12	67)74 1.10
Black + Black Hood	30	(23×3) 69	(20×2) 40	(13×1) 13	30)122 4.06

to the observer, it was decided to obliterate the human scent by the employment of tobacco smoke and repeat the emergence test.

Two puffs of strong cigar smoke were blown into each of the two compartments of the cage. Emergence was then timed for three minutes and recorded on the individual behavior records for each animal. Data have been recorded as previously, except that the population tested is smaller due to interim execution. The results are shown in Table V.

It will be noticed that the scores in Table V correspond rather closely to those of the emergence test made March 4, in spite of the smoke, although in Table V the effect of the smoke may possibly be evidenced by the lesser score of the grays (45:49%). The score of the blacks is several per cent higher in the March 26 test. When the scores for first, second and third emergence are weighted, there is less difference between gray and black, possibly due to grays making more places, and albinos doing better than previously with respect to the blacks. The test was made in the afternoon rather than in the morning. This fact may also have affected the score.

But in spite of all this, the blacks and black hoodeds still make better scores than grays and gray hoodeds and timed emergence is strongly in favor of the blacks as being the less timid. When blacks are compared with grays, the difference for emergents of the 1st minute is not significant. The difference for emergents of the first and second minutes combined is significant as is the difference for emergents of the first, second and third minutes combined.

Fourth Emergence Test

A fourth emergence test was made on April 2. The results shown in Table VI, are in accord with those of the previous tests. An innovation was added to this test. At the time the fourth emergence test was carried out it was noted that most of the rats were dozing. Thus, only the rats that happened to be awake would be recorded, which would bias the results. Hence the observer stirred up the rats in each cage with his gloved hand to awaken them and immediately started timing their emergence. The result was that an excitement factor was thus introduced.

It will be recalled that in the first emergence test the difference in percentage of blacks and grays recorded as "first emergent" was not significant. In the refined emergence test the difference

TABLE V. Smoke-Blocked Emergence Test.

Coat Color	n	Number Emerging	Total Seconds	Average Emerging Time in Seconds	% Emerging During 1st Minute	% Emerging During 2nd Minute	% Emerging During 1st + 2nd Minutes	% Emerging During 3rd Minute	% Emerging During 1st + 2nd + 3rd Minutes
Albino	25	12	788	65.67	28.00	12.00	40.00	8.00	48.00
Gray	40	18 } 27	1883	104.61 } 100.37	10.00 } 10.00	15.00	25.00 } 24.67	20.00	45.00 } 45.00
Gray Hood	20	9 }	827	91.89 }	10.00 } ↑ X	20.00	30.00 } ↑ S	15.00	45.00 } ↑ S
Black	24	18 } 22	1621	90.05 } 89.36	20.83 } ↓ 24.14	33.33	54.17 } ↓ 55.17	20.83	75.00 } ↓ 75.86
Black Hood	5	4 }	345	86.25 }	40.00 }	20.00	60.00 }	20.00	80.00 }

Weighted Scores

	n	1st Emergent	2nd Emergent	3rd Emergent	Total Score
Gray + Gray Hood	60	(9×3) 27	(5×2) 10	(3×1) 8	45/60 = 0.78
Black + Black Hood	29	(7×3) 21	(7×2) 14	(5×1) 5	29/40 = 1.38

in percentage of blacks and grays emerging during the first minute was not significant. This was also true for the smoke-blocked emergence test. In contrast to these results it will be noted that the difference in percentage between grays and blacks emerging during the first minute in the fourth emergence test is highly significant. In none of the other emergence tests is the difference between blacks and grays emerging during the first and second minutes combined highly significant, but in the fourth emergence test this difference is highly significant. It seems probable that these differences between the results of the fourth emergence test when compared with the other three emergence tests, are due to the excitement factor introduced. This would appear to indicate that grays were more disturbed by the stirring than were blacks.

Annoyance Test

The annoyance test consisted of tickling the nose of each rat in its cage with fine brush bristles one inch long fastened to a long wire handle. Data were recorded for the behavior of the individual rats. When these data are summarized as shown in Table VII, it will be seen that grays and gray hoodeds vs. black and black hoodeds made reactions as follows: biting (86:20%), attacking (28:13%), squealing (21:10%), erecting hair (7:0%), snorting (3:0%), chittering (10:7%), hiding (1:0%), nibbling (0:3%). Fifteen per cent of grays and gray hoodeds made no reaction at all as compared with 73% for blacks and black hoodeds.

We may compare the reactions of individuals in the annoyance test with the reactions of the same individuals in the first holding test. If we seek out the records for those individuals that made no reaction to the holding test (H-test) and tabulate their reactions to the annoyance test (A-test) we find that 75% of these rats made no reaction to the annoyance test as well. They had a record of 16% biting, 8% attacking, and 8% nibbling. Under both tests these individuals were relatively undisturbed.

When the figures for the annoyance test are compared for differences in reactions between grays and blacks, biting and no reaction are found to be highly significant. Differences in chittering are of questionable significance.

If we select those individuals that made no reaction to the annoyance test

TABLE VI. Fourth Emergence Test.

Coat Color	n	Number Emerging	Total Seconds	Average Emerging Time in Seconds	% Emerging During 1st Minute	% Emerging During 2nd Minute	% Emerging During 1st + 2nd Minutes	% Emerging During 3rd Minute	% Emerging During 1st + 2nd + 3rd Minutes
Albino	25	8	612	76.50	12.00	16.00	28.00	4.00	32.00
Gray	39	18 } 27	1413	78.50 } 75.59	20.51 } 20.34 ↑	12.82	33.33 } 38.98 ↑	12.82	46.15 } 47.46 ↑
Gray Hood	20	10	628	62.80	20.00 hs	30.00	50.00 hs	0.00	50.00 s
Black	22	17 } 22	954	56.12 } 52.82	50.00 } 53.57 ↓	22.73	72.73 } 75.00 ↓	4.54	77.27 } 78.57 ↓
Black Hood	6	5	208	41.60	66.67	16.67	83.33	0.00	83.33

	n	1st Emergent	2nd Emergent	3rd Emergent	Total Score
Gray + Gray Hood	59	(8×3) 24	(9×2) 18	(4×1) 4	59/46 0.78
Black + Black Hood	28	(10×3) 30	(4×2) 8	(5×1) 5	43/28 1.54

regardless of color and tabulate their reactions to the first holding test, we find biting 19%, attacking 3%, squealing 72%, laying ears back 28%, snorting 3%, chittering 6%, urinating 31%. None of these animals defecated.

The records of these relatively undisturbed individuals in the holding test (as selected by their undisturbed reactions to the annoyance test) may be compared with the reactions of the individuals to the holding test selected on the basis of their having attacked and bitten in the annoyance test. The holding test records of animals that made no reaction to the annoyance test vs. the holding test records of animals that bit in the annoyance test give biting (19:59%), attacking (3:38%), squealing (72:69%), opening mouth (0:3%), laying ears back (28:55%), snorting (3:14%), chittering (6:7%), urinating (31:59%), defecating (0:69%), whining (0:31%), no reaction (28:3%). It will be seen that those animals chosen on the basis of disturbance in the annoyance test are much more disturbed in the holding test than are animals chosen on the basis of having made no reaction to the annoyance test.

If figures for the holding test of individuals that made no reaction to the annoyance test are compared with figures for the holding test of individuals that bit in the annoyance test, we find that differences in percentage of biting and of attacking are highly significant. Differences in laying ears back, urinating and no reaction are significant.

These comparisons indicate that the individuals most disturbed in the holding test are largely the same animals as are disturbed in the annoyance test, and that the animals undisturbed in the holding test are largely those undisturbed in the annoyance test.

Thus, we are dealing with individual similarities of reaction called forth by diverse situations indicating a constancy of behavior basis in the individual. Such a finding is commonly encountered by other investigators and was assumed in these studies.

TABLE VII. Annoyance Test.

Annoyance Test				Comparison of H vs. A tests			
				All Colors			
Color of Segregates	Gray + Gray Hood	Black + Black Hood	Significance of Difference	H records when A=0	A records when H=0	H records the same as A rec.	Significance of Difference
Number of Rats	67	30		32	12	29	
% Biting	86	20	hs	19	16	59	hs
% Attacking	28	13	x	3	8	38	hs
% Squealing	21	10	x	72	0	69	–
% Opening Mouth	0	0	–	0	0	3	–
% Erecting Hair	7	0	–	0	0	0	–
% Laying Ears Back	0	0	–	28	0	55	s
% Snorting	3	0	–	3	0	14	x
% Chittering	10	7	s?	6	0	7	x
% Nibbling	0	3	–	0	8	0	–
% Hiding	1	0	–	0	0	0	–
% Urinating	*	*	–	31	*	59	s
% Defecating	*	*	–	0	*	69	–
% Whining	0	0	–	0	0	31	–
% No Reaction	15	73	hs	28	75	3	s

*Could not be determined.

Garlic Test

It had been noted previously that no rat of this series liked the smell of an onion and it was believed from untimed observations that albinos were less sensitive, or at least made less response to having a piece of onion held before the nose, than did rats of other coat colors.

Hence it was decided to time the repulsion reactions of individual rats to a piece of garlic (*Allium sativum*). The test piece was fastened to the end of a long wire and approached to within about 2 mm. of the rat's nose. Timing was with a stopwatch.

Mrs. Wilkinson (caretaker) reported that Wistar albinos, as compared with other rats in the laboratory hesitate a long time, rather bewildered "as though they didn't know what it was all about" when one offers them a piece of food. She stated that other rats sniff for an instant and either take the food if they like it, or if they don't like it, they back away from it. Both Miss Meeser (Asst. Curator of the Colony) and Mrs. Wilkinson aver that when rats have tasted

something they do not like, they may push the floor away in front of them with both paws, or they may run along rubbing their mouths on the floor.

If one examines the results of this garlic test, shown in Table VIII, one finds that 71.43% of albinos backed away after sniffing the garlic for an average of 9.87 seconds, as compared with 50.91% of grays and gray hoodeds that backed away after an average of 4.28 seconds, and also as compared with blacks and black hoodeds 89.28% of which backed away from the garlic after an average of 5.48 seconds. The smelling and then backing away appears to be a definite olfactory test, the animal backing away because he does not like the odor of allyl sulphide $(C_3H_5)_2S$.

When the difference in percentage of grays that sniffed the garlic and backed away are compared with the percentage of blacks making the same reaction, the difference is found to be highly significant.

4.76% albinos, 18.92% grays, 22.22% gray hoodeds, 0% blacks, and 28.57% black hoodeds attacked the onion in average times as follows: 1.00 secs., 2.00 secs., 2.25 secs., 0.00 secs., and 1 sec. The reactions of these animals are less understandable. Did they quickly smell the garlic, and attack it because they hated the odor, or did they attack because they saw a strange object quickly appear before their faces, not having received or interpreted the odor at all? Indeed, there may be mixed motives represented in this protocol.

The difference in behavior between blacks and grays here is not significant.

23.81% albinos, 16.23% grays, 11.11% gray hoodeds, 4.76% blacks and 0.00% black hoodeds bit the garlic after sniffing for the following average times: 3.60 secs., 4.67 secs., 5.00 secs., 4.00 secs., and 0.00 secs. respectively. This reaction appears to consist of careful olfactory testing followed by the desire to test the taste of the garlic as possible food. However, this group may possibly contain animals that finally became angry enough to bite the garlic although not exhibiting actual attack. The differ-

TABLE VIII. Garlic Test.

Coat Color	n	% Backed away after Av. time in seconds		% Attacked after Av. time in seconds		% Bit garlic after Av. time in seconds		Miscellaneous reactions after time in seconds
Albino	21	(n=16) 71.43% 9.87 secs.		(n=1) 4.76% 1.00 secs.		(n=5) 23.81% 3.60 secs.		
Gray	37	(n=21) 56.76% 4.09 secs.	(n=28) 50.91%	(n=7) 18.92% 2.00 secs.	(n=11) 20.00%	(n=6) 16.23% 4.67 secs.	(n=8) 14.54%	1. jumped back 4. fled 1. grabbed garlic
Gray Hood	18	(n=7) 38.89% 4.86 secs.	4.28 secs.	(n=4) 22.22% 2.25 secs.	2.00 secs.	(n=2) 11.11% 5.00 secs.	5.75 secs.	3. rubbed nose 1. ran 1. grabbed garlic 3. opened mouth 5. opened mouth
Black	21	(n=20) 95.23% 6.15 secs.	n=25 89.28%	(n=0) 0% 0.00 secs.	(n=2) 7.14%	(n=1) 4.76% 4.00 secs.	(n=1) 3.57%	
Black Hood	7	(n=5) 71.43% 2.80 secs.	5.48 secs.	(n=2) 28.57% 1.00 secs.	1.00 sec.	(n=0) 0.00% 0.00 secs.	4.00 secs.	
Significance of Gray vs. Black difference in percentage		hs		x		x		

ence in time between this reaction and the attack make them appear distinct as is shown in Table VIII. However, examination of the figures reveals the fact that there is no significance in the difference between the reactions of blacks and grays.

Curiously enough, the grays and gray hoodeds are still indicated as wilder rats than the blacks and black hoodeds by the following analysis: although 50.91% of grays backed away from the garlic as compared with 89.28% of the blacks, still it took the blacks an average of 1.20 seconds longer before they reacted. Furthermore, 20.00% of grays and gray hoodeds attacked the garlic as compared with 7.14% of blacks and black hoodeds. If the miscellaneous reactions are credited, the grays and gray hoodeds are found to be still much more wild than indicated by these figures.

But a quite unexpected result is also derived from this test: 71.43% of albinos require 9.87 secs. before backing away from the garlic. Combined grays and blacks give 66.26% backing away after 4.85 secs. This would seem to indicate very definitely that the albino rat is much less responsive than the pigmented animals.

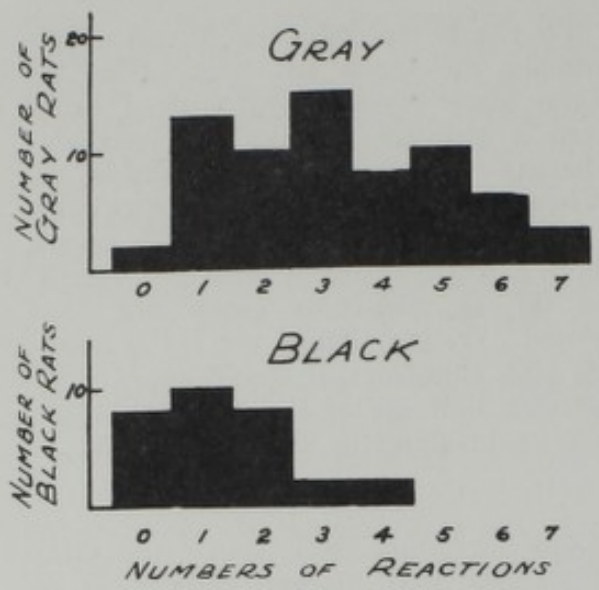
To check this observation on other animals, the garlic was held before 10 Hatai black hoodeds that backed away from it after an average of 7 seconds, whereas a corresponding number of Wistar albinos never did back away from it, but after a time, (about 15 secs.) three of them tested it with their teeth. So far as coat-color genes are concerned (Wistar albinos are Hatai hoodeds plus albinism), it would appear that extreme dullness of the olfactory sense is brought about by the albino gene.

Discussion

The foregoing data have given clear indications that marked differences in behavior exist between gray and black segregates, but the tests do not separate animals of the two coat colors sharply. With any "trait" as fluid and pervasive as temperament, even if differentiated by a single gene substitution, we would not expect any such division. Wild animals are distinguished from tame animals not by a single reaction, but by a cluster of reactions, by a tendency to react more violently with excitement. Many cases have been reported in the literature wherein the presence of a gene is unmistakable but with its expression varia-

TABLE IX. Data of the First Holding Test. Small numbers identify individual rats. A dot beside the identification number indicates a backcross animal. All others are F_2 animals. × indicates reaction made.

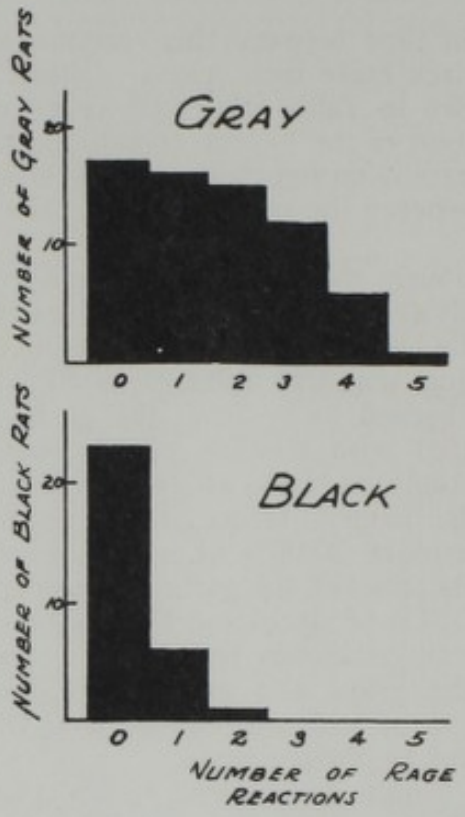




TOTAL REACTIONS COMPARED

Figure 2

Histograms for comparing the numbers of reactions per individual among gray and black hybrid rats in the holding test.



RAGE REACTIONS PER INDIVIDUAL

Figure 3

Histograms for comparing the number of rage reactions per individual among gray and black hybrid rats in the holding test.

ble — sometimes over a considerable range.

In this experiment, the grays contain individuals some of which carry the black gene in one dose, and others of which do not carry the black gene at all. The blacks on the other hand, are all homozygous for the black gene, because black is a mendelian recessive, and hence the black population is genetically more uniform. Thus, if behavior trends are correlated with coat-color genes, the blacks should show a more homogeneous group of behavior reactions, all having very low wildness scores unless influenced by association with wild litter mates.

In the wild individuals there is greater chance of showing taming effects due to a peaceful laboratory environment, than there is of individuals tame by nature becoming wild. And because the naturally wild individuals are largely grays, this environmental influence should also tend to make greater variability among grays.

The raw data of the first holding test have been arrayed in Table IX. If the various numbers of reactions made by different rats (regardless of type of reaction) are plotted against the number of individuals making each consecutive number of reactions, we find a relatively wider distribution (from 0 to 7 reactions) for grays and a more restricted distribution (from 0 to 4) for blacks. These facts are shown graphically in Figure 2.

When these data are examined statistically* it is found that for the gray distribution the mean is 3.2 with standard error of 0.2. The standard deviation is 1.8. $\beta_1 = .07$. $\beta_2 = 2.12$.

The value of β_1 for this sample at the

*Symbols used in these comparisons are as follows:
β_1 (beta$_1$) is a measure of skewness of the distribution function. (Pearson)
β_2 (beta$_2$) is a measure of kurtosis (flatness or peakedness). (Pearson)
s is the standard deviation of the sample. (Fisher)
σ (sigma) is the standard deviation of the theoretical distribution.
t is "Student's" distribution as modified by Fisher, used for the purpose of testing the critical value of differences between means.

two per cent point is .424 so that we would expect a normal curve to agree with the distribution. (See Pearson,[3] vol. II, p. 224).

A normal curve fitted to these data gives a value of chi-square of 4.87 and entering the table with 4 degrees of freedom (leaving 6 less mean plus standard deviation or 4 degrees). Since the end values were combined to increase the frequencies to at least nine, $P = 0.30$, which is satisfactory, according to Fisher, because it lies between 0.9 and 0.1.

The blacks have a mean of 1.3 ± 0.2. The standard deviation is 1.1. $\beta_1 = 0.47$. $\beta_2 = 2.88$.

In this case the values are such that a normal curve would fit the population. However, it was not satisfactory to fit a normal curve to the data owing to lack of number of divisions.

When we compare the mean for grays with the mean for blacks we find, using Fisher's terminology, $s = 0.1474$, $t = 42.6180$, $P < .001$. Hence the difference is highly significant. This curve fitting has been carried out to see if the data represent a normal distribution, in which event the tests for significance are more accurate than if they do not represent a normal distribution.

By inspection of the original data it will be seen that such reactions as squealing, whining and defecating are very commonly found in both grays and blacks and hence may not be good indications of temperamental differences. In fact, they may actually be extraneous to the general group of reactions associated with what may be called rage. Chittering and opening the mouth are too rare to be of much value.

If we plot the remaining data (i.e., those for biting, attacking, laying ears back, snorting, urinating) in order to isolate for comparison the rage cluster of reactions, we find the facts depicted in Figure 3. Both the gray and black curves are moded at 0. Blacks fall off sharply, there being but one rat making as many as two rage reactions. On the contrary, the gray curve continues high, there being 16 rats making one rage reaction, 15 rats making two rage reactions, 12 rats making three rage reactions, 6 rats making four rage reactions, and 1 rat making five rage reactions. Thus, by removing those reactions not supposed to be associated with rage, the differences between grays and blacks are more accentuated than when we considered all reactions regardless of type.

When we study the distribution of these reactions for grays we find mean $= 1.6 \pm 0.1$. Standard deviation $= 1.3$. $\beta_1 = 0.14$. $\beta_2 = 2.16$. The theoretical population has probably a Pearson Type I curve.

The black distribution has a mean of 0.3 ± 0.1. The standard deviation is 0.5. $\beta_1 = 3.14$. $\beta_2 = 5.20$. The theoretical population probably has a Pearson Type I curve. (See chart on p. 66. Pearson,[3] vol. I).

The means for grays and blacks may be compared. Here it is found that $s = 0.2147$, $t = 40.3964$, $P < .001$. Hence, the difference between the means is highly significant.

Another difference observed between gray and black rats is the intensity of reactions made. The squeal of the gray rat is frequently loud and prolonged; that of the black, a short cry of no great intensity which may degenerate into a protesting whine. Urinating frequently consists of a strong spurt or stream in the gray as compared with the slow emission of one or several drops in the black. Defecation frequently includes the extrusion of three to five boluses in grays, but more often of a single bolus in blacks. Biting in the gray rat may entail a series of six or seven forceful bites delivered with machine-gun rapidity; in the black it is often a single, weak nip.

Summary

1. Two holding tests, four emergence tests, and an annoyance text give similar results indicating the greater wildness and savageness of animals bearing a gray coat compared with those having a black coat in a population of 125 segregates of crosses of tame albino (carrying black) with wild gray Norway. It is likely that

pleiotropy accounts for this association between coat color and temperament.

2. Comparison of the annoyance test with a holding test shows the most annoyed and the most undisturbed rats in each test to be largely the same individuals, as would be expected, if the basis of wildness and savageness remains relatively constant in the individual under different situations.

3. A garlic test suggests differences between gray and black segregates in the sense of smell. It also suggests that the albino gene has a profound dulling effect upon that sense.

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IV

DR. KING'S SO-CALLED "DOMESTICATED GRAY" RATS.

Written in 1939

In 1919 Dr. King set out with the express purpose of "domesticating" the wild gray Norway rat, a project that Dr. Hatai had discontinued when he returned to Japan several years before.

Dr. King always claimed that she was accomplishing this purpose in a remarkable fashion, as when she reported that "After 14 years of life in captivity the behavior of gray rats had changed so greatly that many of the obnoxious traits exhibited by the early descendants of feral animals had disappeared" or when she stated "Gray rats, therefore, can now be used for all forms of experimental work."

Again she says,"More recently, a number of young gray rats were given to Miss Meeser for taming, and she succeeded in making them as gentle as are stock albinos".

"At the twenty-fifth generation gray rats had lost the high nervous tension and fear of man displayed by individuals in early generations. Females then took excellent care of their young and would serve as foster mothers if certain precautions were taken. Two of the outstanding traits in rats of early generations still persisted; adults continued to show antipathy to strangers placed in their cage, and exceptionally large rats, particularly males, were yet prone to attack small individuals of the same sex. Gray rats of later generations could be rendered as tame as are stock albinos if they were handled frequently during early life. It was then possible to use these rats for any kind of experimental work".

A dream at the Wistar Institute had been that possibly if albino mutants occurred in King's wild gray Norways, as they had done in Hatai's grays, they would become tame quicker than the grays under similar conditions of domestication. Accordingly, a note of Dr. Donaldson's dated Dec. 21, 1929 says that Dr. King reports "Albino mutants are tamer than their gray ancestor, Noticeably so."

It is my belief that such statements are in the main simply not true. Unfortunately, they have given outsiders, and especially experimental psychologists, the erroneous impression that Dr. King's domestication efforts have been eminently successful, and that her "domesticated" rats may now be handled quite as readily as Wistar albinos or other tame laboratory albino stocks.

Whereas, there may be a slight difference in degree of fear between the first generation in captivity and their descendants today, it is a noteworthy fact that members of the 55th generation in captivity still thrash and huddle in the farthest corners of their cages with fright when one approaches. On various occasions I have seen Dr. King throw a large ether-soaked bundle of cotton into their cages in order to subdue them enough to permit their capture by means of tongs. These rats still struggle, shriek and bite continuously at the tongs when lifted out of their cages. They may fly out of their cages to attack the observer, and frequently do attack if they escape to the floor.

According to Miss Meeser's experience, these gray Norway rats of the 55th generation can never be tamed except by daily handling, and then only by beginning the handling routine on suckling rats before their eyes are open. Even then many of the so-called "hand-tamed" individuals will permit no one except Miss Meeser to handle them.

The truth seems to be that the net alteration in the germplasm controlling temperament and behavior trends during more than 50 generations of captivity is very slight indeed.

What changes have actually taken place are still subject to the suggestion of Hall as being partly due to unconscious selective breeding when he says, "It is not inconceivable that the parents of each successive generation were the least wild animals."

I am also inclined to consider Stone's question, "What portion of the behavior change reported for these rats might just as well have been obtained in the first laboratory generation if they had been handled by caretakers who already possessed the same interest, skill and innocence of being bitten that was probably present by the time the tenth generation arrived"?

From my limited experience with these captive gray Norway rats, by no stretch of the imagination could I call any of them "domesticated" animals. I draw attention to the true state of their behavior because these rats provide the standard with which the anatomy and behavior of other strains are to be compared in my papers on the subject of behavior in rats.

In contrast with her declarations concerning the tameness of "domesticated" gray Norways, King has said extremely little about the behavior of other strains, including the mutants derived from the gray Norway.

In her contribution to the Sixth International Congress of Genetics Dr. King had a special section on "behavior" in gray Norways, and although she describes the mutants "affecting color and structure of the hair" in detail, nothing is said about the altered behavior of mutants. From all I can learn, it appears that Dr. King was not in any way concerned with the behavior of the mutants.

As a matter of fact, Dr. King's notoriously aggressive rat handling techniques kept all except the most phlegmatic in a constant state of nervous tension which prevented any accurate impressionistic description of their

comparative tameness and docility trends in her colony. She attempted no behavior tests. Only in the quiet of Miss Meeser's colony procedure could the natural differences be adequately assessed.

Of mutants from the gray Norway, I can observe as others in the laboratory have done, that stub, curly and albino are not only as wild and savage as the source stock., but even more so. Piebalds and Cinnamons may be slightly less wild than the gray. In contrast to all these, the blacks are quiet and gentle.

The albino-waltzer is very nervous, but much more easily tamed than is the albino. It is really strange that Dr. King does not seem to have noticed these differences, or at least, did not give them enough consideration to mention them in any of her papers, so far as I have been able to learn.

Dr. King states that "Black mutants have bred true until this Spring when members of a litter were found to have numerous white hairs scattered throughout the coat." This experiment extended over a period of 6 years or about 13 to 14 generations of naturally tame blacks, and yet she makes no mention of their behavior. I have observed seven unhandled adults of the last generation and can testify to their tameness.

Again King says, "During the period that the Norways have been under investigation, six different heritable mutations have occurred all affecting the hair." The only allusion to behavior is the following: "Weight determinations of various body organs, made by Dr. Donaldson, and behavior of the individual indicate that these Albinos, have the characteristics of wild Norway rats. They carry genetic factors for gray and self." In spite of this statement, Dr. King has told me that a number of the mutant albinos carried piebald and a few of them carried black. Under these complicating circumstances it would have been difficult to have assigned a definite behavior trend to one or more of the three color genes involved.

In King's 1939 article there is mentioned the occurrence, as a mutation, of cinnamon rats. This or a similar variation had been described previously by Patterson. Dr. King combined her cinnamon with non-agouti black (which she tells me was her black mutant stock) to produce chocolate double recessives. No mention was made of their extremely tame behavior, but I have held unhandled adults of this chocolate strain in my bare hands with perfect ease. I would estimate them to be about as tame as their black ancestral stock.

V

Growth, 1943, 7, 83-95.

SOME VARIATIONS IN BASAL METABOLIC LEVELS OF RATS*

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A. INTRODUCTION

It has been shown by Hatai and Donaldson (Donaldson, 1924) that the weight of the thyroid gland of the laboratory albino rat is relatively smaller for a given body length than that of the wild gray Norway rat from which the albino variety was derived. Donaldson collected extensive dissection data up to the time of his death in 1938. An examination of these data (Keeler and King, 1942) shows a similar reduction in the relative size of the thyroid to accompany several coat color genes that happen to be present in most laboratory albinos. One of these genes is the black gene.

Observations of behavior (Keeler, 1942) revealed variations in the response to given situations. Those variations which accompanied the presence of the black (non-agouti) gene are quite outstanding and are oriented in the direction of sociability and tameness as well as a reduction of activity when compared with the wild gray coat color variety. It appears most probable that these are pleotrophic effects of the black gene rather than manifestations of genes residing in the same chromosome with the black gene.

This reduction in the weight of the thyroid accompanied by a reduction in activity obviously suggests an alteration in thyroid function as the mechanism by which the black gene modifies behavior because the association of thyroid hypofunction and reduced activity is well known. The present experiments were undertaken to determine the basal metabolic levels (average basal metabolism for each variety) for rats of several coat color constitutions and to learn whether any correlation existed between the size of thyroid or coat color and the basal metabolism. Heart rate and blood pressure were also studied since they frequently exhibit changes associated with variations in thyroid function.

*Aided by a grant from the Women's Auxiliary of the Lankenau Hospital Research Institute.

B. Materials

The rats studied consisted of 12 Wistar albinos, 14 F_2 hybrids of assorted coat colors derived from a cross between Wistar albinos and gray Norways (see Figures 1 and 2), six animals of assorted coat colors

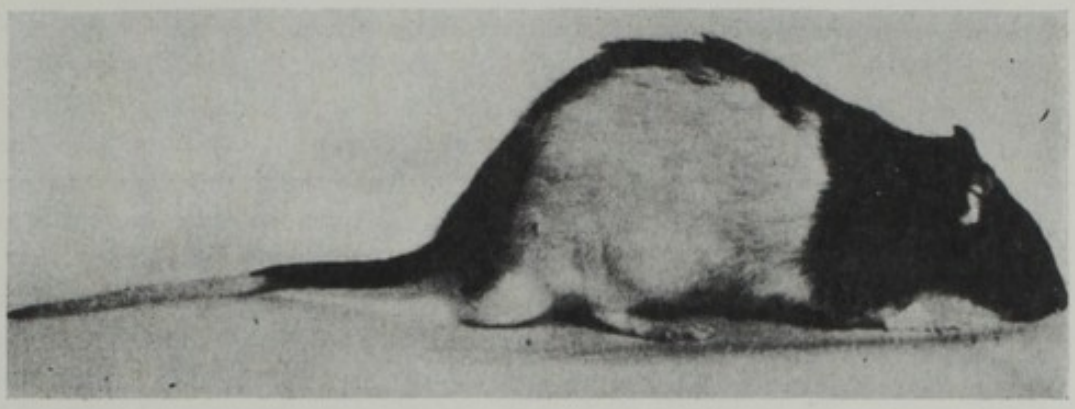


FIGURE 1
Adult Male F_2 Hybrid Piebald Gray Rat. Note Piebald Markings on Tail

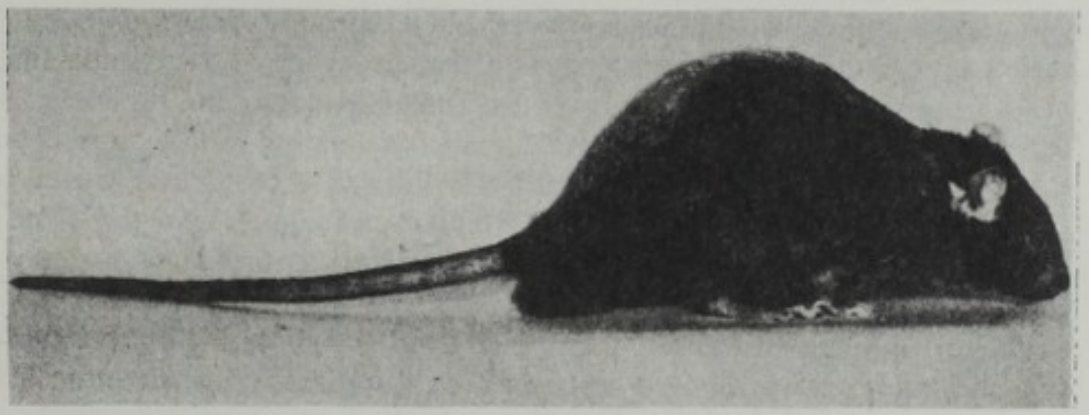


FIGURE 2
Adult Male F_2 Hybrid Gray Rat

segregating for black and hooded, four hairless albinos, and three curly hooded piebald blacks.

C. Apparatus

The metabolism apparatus was essentially that described by Schwabe and Griffith (1938). It consists of a closed system containing oxygen at atmospheric pressure. Any carbon dioxide exhaled by the animal is

quickly absorbed by a solution of barium hydroxide so that the oxygen consumed by the animal tends to cause a reduction in the pressure. The decrease in pressure is never realized, for water siphons over from the manometer system to reduce the volume in which the gas must act. A writing point floated on the surface of the water manometer produces a permanent record of the volume change upon the kymograph.

To this Schwabe-Griffith apparatus there was added a Wheatstone bridge which permitted conductrimetric titration of the barium hydroxide at any instant without necessitating the stopping of the apparatus or the removal of any of the solution. This bridge (Griffith, 1940) has two platinum electrodes immersed in the barium hydroxide solution of the set of bulbs which are opened to the animal chamber during the experimental run. By use of a 1000 cycle microhummer and earphones the conductivity could quickly and accurately be obtained.

The systolic blood pressure was measured using the indirect method upon the tail (Byron and Wilson, 1938) (Williams, Harrison and Grollman, 1939) in which the circulation of the tail is abruptly arrested by inflating an air cuff about the root of the tail. The pressure in this cuff is gradually reduced to the systolic level at which point blood is able to flow into the tail but is unable to leave. This results in an increase in the size of the tail which is detected by a water plethysmograph. Minor modifications were introduced by using glass cuffs throughout and a 25 cc. syringe instead of a leveling bulb. Beer cans with a tapered neck and with the bottoms removed proved excellent animal holders during these experiments.

The heart rate was measured by an ordinary hospital electrocardiogram machine fitted with miniature cuffs.

D. Method

Adult male rates (Davis and Hastings, 1934) were placed on the standard laboratory diet and not tested for at least a week after arrival. Measurements were repeated at intervals of about a week to obtain a check on the first values. The afternoon before the animal was to be tested all food was removed from the cage and the rat allowed to fast for at least 17 hours before the measurement of the metabolism. All experiments were performed between 10 A.M. and 4 P.M. to eliminate any diurnal variations (Horst, Mendel, and Benedict, 1934).

Since great differences in metabolic rates have been demonstrated between such seemingly similar conditions as dozing and sleeping

(Davis and Hastings, 1934), it was deemed necessary to place all animals under identical conditions. Light anesthesia produced by subcutaneous injections of Nembutal (sodium pentobarbital) 36 milligrams per kilogram body weight (Barlow and Gledhill, 1933) proved very satisfactory (Griffith and Farris, 1942). About 20 minutes after the injection the animal became totally relaxed and in this condition was placed into the glass animal chamber and after several minutes the experiment was begun. About one hour after the injection the rat began to arouse, slowly regaining normality with no noticeable after effects. That this anesthetic lowers the oxygen consumption only slightly (Chen, Anderson, and Leake, 1930) was substantiated by our results with the Wistar albinos as compared with standard values. Fresh solutions of Nembutal, concentration 10 mg. per cc., were prepared daily. The dosage as well as the surface area (Lee, 1929) was calculated from the weight of the animal.

The kymograph furnished a permanent record of the oxygen consumption rate from which the basal metabolism was calculated. The conductivity of the barium hydroxide was measured before and after the experiment and from these values the volume of carbon dioxide exhaled was computed. The respiratory quotient, obtained from the CO_2 and O_2 volumes, served as a check upon the correct functioning of the apparatus, results only being accepted when the quotient was about 0.72.

Immediately upon completion of the metabolism measurement the still drowsy animal was transferred to the warming box where it was subjected to a temperature of 40°-42°C. for 10 minutes. The beer can animal holder mentioned above was also placed in the warming box to reduce heat losses as much as possible when the rat was later placed into it. After this warming period which produces vasodilation the animal was arranged in the holder so that the nose protruded through the mouth of the can enabling it to breathe freely. The tail was threaded through the pressure cuff and plethysmograph following which the systolic blood pressure was determined as described above. The first reading was taken rapidly to obtain an approximate value after which a second accurate reading was made. This accurate value was then checked by a second person to reduce errors. All of these readings should be taken as rapidly as possible to eliminate any variations due to changes in body temperature. Unanesthetised animals may be used if they are trained to remain quiet in the holder, but we found such

values to differ but slightly from those obtained upon anesthetised animals.

The heart rate was determined by electrocardiography employing the same machine and method as for human work but with miniature electrodes adapted to the rat's legs. Again, anesthetised animals were used to keep the observational conditions uniform and to prevent distorted results due to any excitement.

E. Calculations and Results

The volume of oxygen consumed by the animal must be corrected to standard temperature and pressure before the metabolism can be calculated. The calorific value of oxygen used here is 4.702 Calories per liter (Benedict, Horst, and Mendel, 1932). This value is about three per cent lower than the value used for human metabolism, but is more accurate for work with rats.

The specific conductance of a cell is known to depend upon the size and character of the electrodes. Since the size of the electrodes is rarely exactly one square centimeter, and since the characteristics of platinum-blacked plates may change slightly with use, a cell constant must be determined and checked frequently using 0.01 demal potassium chloride solutions (Parker and Parker, 1924). The specific conductance of the barium hydroxide solution can be calculated from its resistivity and, after correcting for temperature variations, the normality of the solution can be determined. The temperature correction for this apparatus and the temperature range of these experiments was 200 $k_0(28°—T°)$ where k_0 is the observed specific conductance. From the normality (Leopold and Luck, 1933) and the volume of barium hydroxide in the absorbing bulbs, the amount of carbon dioxide excreted may be calculated.

The results are arranged to show the experimental results and the metabolisms derived from these data. They are grouped according to coat color characteristics and breeding (Figure 3, Table 1, Figure 4).

F. Discussion

A consideration of Figure 1 shows a definite variational trend between the coat color groups. This is surprisingly oriented in the direction opposite from that of thyroid size and degree of activity. In both the inbred and hybrid populations the gray rats are operating at a lower metabolic level than are the blacks of the same stock. The piebald

OXYGEN CONSUMPTION AND METABOLISM

1 mm. rise of kymograph pointer = 1.234 cc. Oxygen

$$\text{Oxygen at } STP = 1.234\ (\Delta h) \times \frac{P}{760} \times \frac{273.1}{T} \text{ cc.}$$

Calorific value of Oxygen = 4.702 Calories per liter

$S = 12.54\ Wt^{0.66} \times 10^{-4}$ square meters

$$\frac{BM}{S} = \frac{\text{.cc. } O_2}{1000} \times 4.702 \times \frac{1440 \text{ mins.}}{t} \times \frac{1}{S} \text{ Calories per day per square meter}$$

CARBON DIOXIDE EXCRETION AND RESPIRATORY QUOTIENT

$$R_c = R_s \frac{L-l}{l};\ K_c = \frac{1}{R_c};\ k = K_c C;\ k = \frac{1}{R_s} \times \frac{l}{L-l} \times C$$

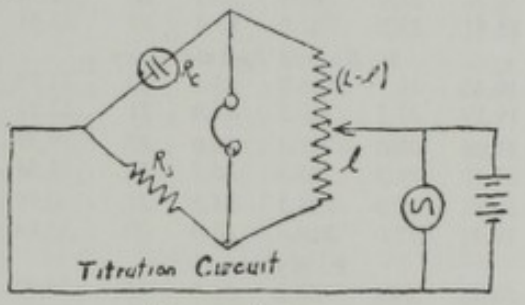
The specific conductance varies with the concentration of the solution and the amount of carbon dioxide absorbed may be calculated from the decrease in the concentration of the barium hydroxide.

milliequivalents $Ba(OH)_2$ reacting = (volume $Ba(OH)_2$ in system) $(N_f - N_o)$

1 milliequivalent $Ba(OH)_2$ = 11.207 cc. CO_2 at *STP*

$\therefore$ volume CO_2 absorbed = $(N_f - N_o)$ (volume) (11.207)

$$RQ = \frac{\text{volume } CO_2}{\text{volume } O_2}$$



KEY TO SYMBOLS

STP	Standard Temperature and Pressure	C	cell constant
Δh	rise of pointer on kymograph	R_s	standard resistance
P	atmospheric pressure in mm. Hg	R_c	resistance of $Ba(OH)_2$ in the cell
T	temperature in degrees Kelvin	$\frac{L-l}{l}$	ratio of lengths of resistance wire
BM	basal metabolism	K_c	conductivity of the $Ba(OH)_2$
S	body surface in square meters	k	specific conductance
t	duration of the experiment in mins.	N_f	normality of $Ba(OH)_2$ after test
RQ	respiratory quotient	N_o	normality of $Ba(OH)_2$ before test

FIGURE 3

gene seems to have the effect of lowering the metabolic level both in the case of the black hybrids and gray inbred animals. In the black hybrids its effect in one dose (belly-spotting) and in two doses (piebald) is almost a mathematical subtraction. However, the reversal of these results in the hybrid piebald grays versus the hybrid grays must be considered and eliminated before any definite statement can be made.

TABLE 1

THE BASAL METABOLISM OF RATS WITH VARIOUS COAT COLOR CONSTITUTIONS AND THE DATA FROM WHICH IT WAS DERIVED

Rat No.	Date	Weight	$\frac{1}{S}$	T	P	Δh	t	BM	Cal./ day/m^2	Rat avg.	Group avg.
					Inbred Piebald Gray						593.9
1	7-28	354.4	23.55	28.2	763.3	82.1	23	27.15	639.4		
	8- 4	357.8	23.42	28.0	762.0	85.9	28	23.31	545.9		
	8-11	374.9	22.77	28.0	760.5	85.1	25	25.81	587.7	591.0	
2	7-28	300.6	26.00	28.5	763.3	84.4	27	23.75	617.5		
	8- 4	320.0	25.04	28.0	762.0	85.7	27	24.12	604.0	610.7	
3	8- 4	340.1	24.14	27.9	762.0	83.9	27	23.89	576.7		
	8-11	355.3	23.51	27.0	760.5	84.5	26	24.73	581.4	579.1	
4	7-28	270.8	27.68	29.2	763.3	60.4	23½	19.48	539.2		
	8-15	307.0	25.67	28.0	763.6	86.5	26	25.33	650.2	594.7	
					Inbred Gray						678.5
10	8- 4	264.5	28.07	28.0	762.0	79.7	25	24.22	679.8		
	8-11	282.2	27.00	27.0	760.5	85.7	26	25.08	677.2	678.5	
					Inbred Black						803.0
20	7-28	326.1	24.76	28.0	763.3	85.2	20	32.42	802.7		
	8- 4	344.1	23.97	28.0	762.0	83.8	19	33.51	803.2	803.0	
					F_2 *Hybrid Piebald Gray*						629.2
30	7-24	487.8	19.45	29.7	765.5	83.5	19	32.72	636.3		
	8- 6	481.8	19.59	27.5	762.3	88.6	21	32.12	629.2	632.7	
31	7-30	427.0	21.06	29.0	761.3	86.0	22	29.57	622.7		
	8- 7	423.4	21.17	26.5	765.3	86.2	24	27.54	582.9	602.8	
32	8- 7	455.7	20.25	27.0	765.3	84.2	21	30.70	621.8		
	8-13	465.6	19.95	27.0	764.3	88.0	20	33.64	672.6	652.2	
					F_2 *Hybrid Gray*						518.1
40	7-30	452.8	20.33	29.4	761.0	82.0	25	24.77	503.6		
	8- 7	460.9	20.12	28.0	765.3	86.9	26	26.02	523.4	513.5	
41	7-30	470.2	19.88	29.5	761.0	86.7	26	25.18	500.5		
	8- 7	467.0	19.96	27.5	765.3	89.3	25	27.30	544.9	522.7	
					F_2 *Hybrid Piebald Black*						610.3
50	8- 6	497.5	19.21	27.3	762.3	87.0	20	33.14	636.6		
	8-13	509.6	18.94	28.0	764.3	85.5	21	31.03	587.7	612.2	
51	7-22	367.4	23.05	29.3	763.5	70.8	20	26.99	622.1		
	8- 6	382.6	22.49	28.3	762.8	83.5	24	26.44	594.6	608.4	
					F_2 *Hybrid Spotted Black*						635.2
60	8- 6	401.6	21.85	28.0	762.8	87.6	23	28.97	633.0		
	8-13	417.2	21.36	27.0	764.3	84.7	22	29.44	628.8	630.9	
61	7-10	399.2	21.93	29.1	763.9	89.1	23	29.41	647.2		
	7-22	381.9	22.52	29.1	763.5	74.9	19	28.06	631.9	639.5	
					F_2 *Hybrid Black*						676.3
70	7-22	331.3	24.52	29.8	763.5	84.2	23	27.70	679.2		
	8- 6	345.7	23.90	27.3	762.3	87.6	24	27.81	664.7	671.9	
71	7-10	324.4	24.83	28.5	765.3	81.8	23	27.09	672.6		
	7-22	315.6	25.25	29.7	763.2	25.1	5¾	27.27	688.6	680.6	
					Curly Hooded Piebald Black						702.3
80	7-16	294.8	26.30	30.2	764.3	72.4	20	26.91	707.7		
	7-29	312.8	25.38	29.6	761.4	81.0	23	26.59	674.9	691.3	

TABLE 1 (*Continued*)

Rat No.	Date	Weight	$\frac{1}{S}$	T	P	Δh	t	BM	Cal./ day/m^2	Rat avg.	Group avg.
81	8- 5	315.4	25.26	28.0	764.4	85.9	23	28.47	719.2		
	8-11	335.6	24.33	28.0	760.5	86.0	22	29.64	721.1	720.1	
82	7-14	295.7	26.25	30.0	760.3	86.1	24	27.01	709.0		
	7-16	287.5	26.70	30.4	764.3	83.1	20	25.55	682.2	695.6	
					Wistar Albino						706.1
90	7- 7	320.0	25.04	28.6	760.1	86.6	24	27.32	684.1		
	7-14	343.1	24.01	31.9	759.6	82.1	21	29.22	701.7		
	7-17	335.9	24.32	31.0	765.7	87.9	22	30.20	734.5	706.7	
91	7- 8	240.8	29.70	29.3	757.8	81.3	27	22.65	672.6		
	7-21	247.8	29.19	32.3	760.5	81.9	28	21.88	638.7	655.7	
92	7- 3	332.8	24.46	27.5	762.7	84.8	21½	30.04	734.7		
	7- 8	338.0	24.23	29.4	758.1	81.1	19	32.11	778.0	756.3	
93	7- 7	404.3	21.76	29.2	760.1	84.2	18	35.31	768.4		
	7-17	420.2	21.26	30.1	766.5	84.5	18	35.63	757.6	763.0	
94	7- 7	356.2	23.48	29.7	760.1	83.6	22	28.64	672.4		
	7-17	371.9	22.88	31.0	765.7	88.1	22	30.27	692.6	682.5	
95	7- 7	324.2	24.84	28.5	760.1	76.9	22	26.45	657.0		
	7-21	343.0	24.02	32.0	760.5	83.3	23	27.10	650.9	654.0	
96	7- 7	343.1	24.01	29.8	760.1	84.5	21	30.31	727.8		
	7-17	359.2	23.36	30.0	767.0	84.8	21	30.68	716.7	722.3	
97	7- 3	275.8	27.37	26.9	762.7	81.6	25	24.91	681.9		
	7- 8	271.9	27.61	28.5	758.1	84.9	24	26.69	736.9	709.4	
98	7- 3	360.0	23.53	26.9	762.7	85.4	22	29.63	691.3		
	7- 8	355.9	23.49	29.5	758.7	86.5	23	28.28	664.3	677.8	
99	7- 3	312.8	25.38	27.4	762.7	84.1	22½	28.48	722.9		
	7- 9	314.0	25.32	28.9	761.2	85.5	24	26.96	682.8	702.8	
100	7-17	418.3	21.32	31.0	765.7	83.9	18	35.23	751.1		
	7-21	404.8	21.74	32.1	760.5	88.7	21	31.60	687.1	719.1	
101	7- 3	322.8	24.91	27.5	762.7	81.8	21	29.67	739.0		
	7- 9	319.5	25.06	29.0	761.2	85.9	23	28.25	708.0	723.5	
					F_2 *Hybrid Piebald Gray—Thyroid-parathyroidectomized*						640.1
110	7-30	379.6	22.60	29.0	761.3	78.5	21	28.28	639.1		
	8- 7	389.3	22.26	28.0	765.3	86.8	23	28.80	641.1	640.1	
					F_2 *Hybrid Gray—Thyroid-parathyroidectomized*						623.8
120	7-24	369.0	22.99	29.2	765.7	67.9	20	25.35	582.7		
	8- 7	349.3	23.76	28.0	765.3	84.5	24	26.87	638.3	615.5	
121	8- 7	458.1	20.19	28.0	765.3	87.4	21	31.76	641.2		
	8-13	454.0	20.30	28.0	764.3	84.6	21	30.70	623.2	632.2	

For this reason further studies on larger numbers of siblings are being planned to eliminate the effects of extraneous genetic characteristics. In no case did the metabolism of the grays reach the level of the albino variety, which is really pure bred for black, piebald, and albinism, and only the one black inbred animal surpassed it among the black animals.

Since segregation for the Wistar albino types of metabolism (high) was not noted in the F_2 hybrids, it is probable that the inheritance of a

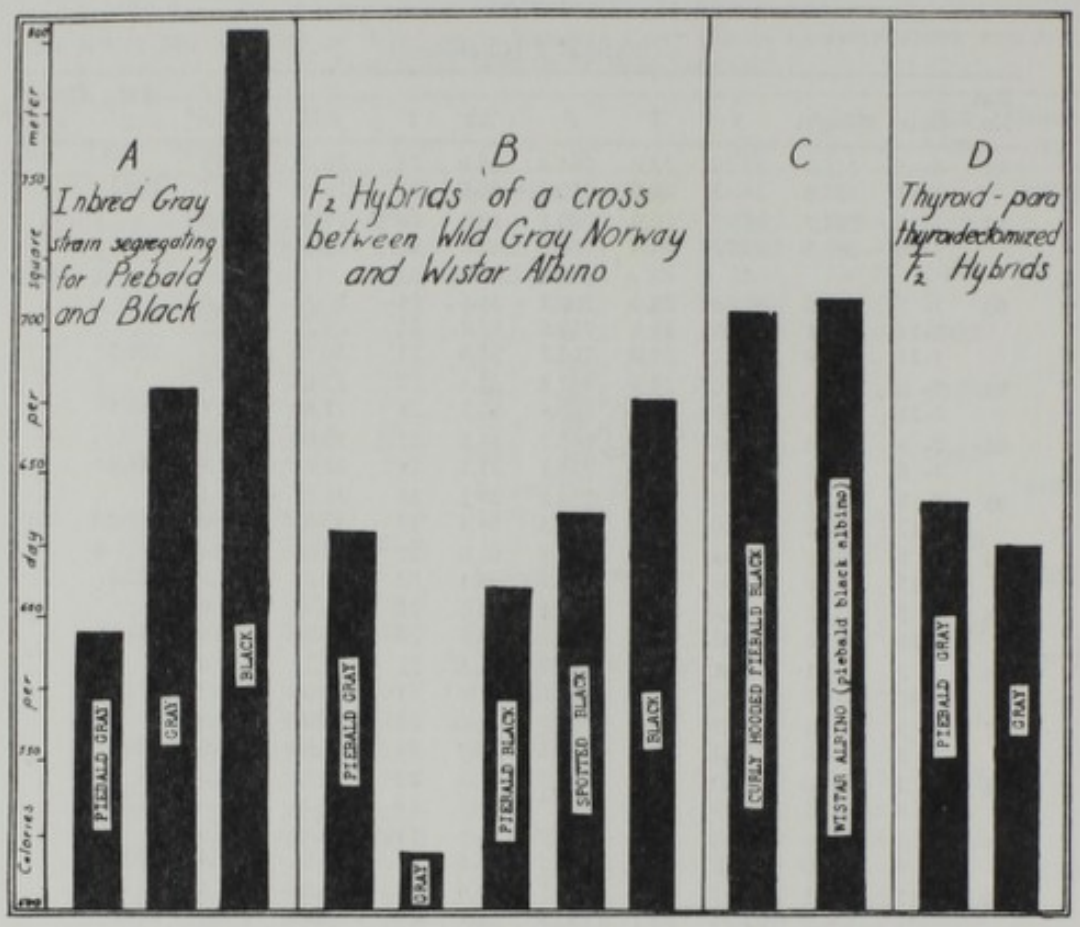


FIGURE 4

AVERAGE METABOLIC RATES OF RATS CLASSIFIED ACCORDING TO COAT COLOR AND BREEDING

high metabolism as contrasted with the low metabolism of the wild gray rat is dependent upon more than one pair of genes. If the heredity of the Wistar albino type metabolism had been dependent upon a difference of but one pair of genes in the total genetic constitution from the wild gray, one would have expected the high metabolic rate to have appeared in one out of four of the F_2 hybrids, which event did not occur.

The association of clinical hyperthyroidism with a normal or subnormal basal metabolism is not an unusual finding in humans, although the cause for this association is not known. Experimental production of hyperthyroidism through repeated injections of thyrotropic hormone (Siebert and Smith, 1929; Marine and Rosen, 1933) at first causes the basal metabolism to increase but, after a few weeks, the metabolism falls to subnormal while the thyroid hyperplasia and the nervous mani-

festations persist. That this is the true explanation here is not known, but at least the picture is the same in both cases. In these rats the possibility that this association of hyperthyroidism with low basal metabolism is the result of pleotrophic effects of the coat color genes must also be considered. At present, however, the mechanism remains unknown and must be clarified by further work.

The occurrence of normal basal metabolisms in the thyroid-parathyroidectomized animals was found to be due to hyperplasia of the thyroid. The operation had been performed without the aid of a dissecting microscope eight weeks before the measurements of metabolism were made. Although at the time of operation it was thought that all of the glandular tissue had been excised, small amounts of hyperplastic tissue with the high type epithelium were found in the histological sections prepared after sacrificing the animals. No parathyroid tissue was present but it is known that the rat can live without them, showing only a calcium deficiency (Schour, Chandler, and Tweedy, 1937).

The albino hairless rats exhibited a higher metabolic level (Table 2)

TABLE 2

THE BASAL METABOLISM OF HAIRLESS ALBINO RATS AND THE DATA FROM WHICH IT WAS DERIVED

Rat No.	Date	Grams Weight	S	T	P	Δh	t	BM	Cal./day/m^2
131	7-23	170.0	36.60	29.0	763.0	69.2	19	27.59	983.5
	7-29	187.8	34.47	30.6	760.4	81.3	22	27.78	957.7
	8-13	241.2	29.67	27.5	764.3	86.9	22	30.15	894.5
132	7-23	162.5	37.60	28.9	763.0	67.2	20	25.49	958.4
	7-29	176.5	35.78	30.6	760.4	83.0	26	24.00	858.7
	8- 5	202.2	32.98	28.0	764.4	83.6	25	25.49	840.6
133	7-23	267.8	27.86	29.1	762.3	70.5	17	31.46	876.5
	7-29	260.8	28.31	30.2	760.4	87.8	26	25.42	719.6
	8- 5	274.1	27.48	28.0	764.4	81.3	24	25.82	709.4
134	7-23	249.8	29.05	29.0	763.0	68.6	17	30.61	889.2
	7-29	248.9	29.11	30.4	760.4	81.2	23	27.42	798.3
	8- 5	265.2	28.03	28.0	764.3	83.7	24	26.58	744.9

than the normal hair-bearing variety as would be expected, since they have lost their insulating coat. However, an interesting trend was noted. The rats tested were 3-6 months old and although they were continually losing more and more hair, the metabolic level continuously *decreased*. The loss of hair is accompanied by the development of numerous dermoid cysts which gradually harden, fall out, and leave empty craters. The skin becomes coarse and hangs in loose folds suggesting a pock-

marked old man. It may be that this heavy, thickened skin permits less and less radiation and evaporation which processes normally account for the greater amount of heat losses. The animal would thus be required to expend less and less energy to maintain the body temperature and the metabolism would decrease.

A study of the heart rates (Table 3) also shows variations associated

TABLE 3
HEART RATES OF SEVERAL VARIETIES OF RATS

Rat No.	beats / min.	Group avg.
	Wistar albino	
94	456	
95	402	430
96	435	
100	456	
	F_1 *hybrid piebald gray*	
31	461	
32	446	454
	F_2 *hybrid gray*	
40	414	
41	360	387
	F_2 *hybrid piebald black*	
50	427	
51	440	434
	F_2 *hybrid spotted black*	
60	410	
61	420	415
	F_2 *hybrid black*	
70	393	393

with coat color. Most marked is the effect of the piebald gene which causes an increase in the rate. Again the difference between one and two doses is noted in the piebald and spotted black rats.

The measurements of blood pressure disclosed no significant differences between animals bearing the various coat color characteristics. The range lay between 110 and 140 with a mode of about 120 mm. of mercury. However, the thyroid-parathyroidectomized animals were markedly hypotensive with an average systolic pressure of only 98 mm. This may indicate that the subtotal removal of the thyroid and complete removal of the parathyroid glands exerts an effect from which the cardiovascular system requires a longer time to recover than does the general metabolism.

G. Conclusions

1. Wild gray Norway rats operate at a lower basal metabolic level than do Wistar albinos.
2. Hybrids between the wild gray Norway and the Wistar albino inherit the lower metabolism of the gray parent.
3. The most important factors in this alteration of basal metabolism are the coat color genes.
4. Because segregation for high (Wistar albino type) metabolism in the F_2 hybrids was not noted, inheritance of this type is probably based upon more than one pair of genes.
5. Our findings of high basal metabolism in the hairless albinos confirms the findings of Benedict. We also find that the metabolism decreases with age and its concomitant hair and skin changes.
6. The heart rate also varies with the coat color.
7. Blood pressure probably requires a longer period of time to return to normal than does basal metabolism following parathyroidectomy and subtotal thyroidectomy.

H. Summary

Experiments upon rats of various coat color characteristics showed variations in basal metabolism and heart rate which appear associated in some manner with the coat color. A decrease in basal metabolism with age is shown by the hairless albino rats.

The work reported here was done at the Lankenau Hospital Research Institute with the technical assistance of Dr. Thomas Garrett, Dr. Theo. Lavine, Dr. M. A. Bennett, Miss Amie Faught, and Miss Grace Jones. Some of the experimental animals were generously provided by Prof. Elmer Roberts and Prof. Sumner O. Burhoe.

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VI

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BIOCHEMISTRY AND TEMPERAMENT IN THE AGOUTI RAT

To the Editor:

I have just received the November, 1942, issue of the Journal of Heredity, and was greatly interested in the paper by Clyde E. Keeler on the Association of the Black Gene with Behaviour in the Norway Rat. I would like to quote a few references, and possible conclusions that may be drawn from them.

(1) Grey rats are more savage than black. (Keeler: Journal of Heredity, Nov., 1942.)

(2) White rats have sufficient extra adrenal tissues to survive extirpation of the glands. (Hoskins: *Endocrinology*, page 20.)

(3) Bloch and his co-workers suggested that all pigmentation is due to the presence of a specific oxydase in the skin, which forms melanin from 3-4-di-hydroxyphenyl-alanine. They expressed the belief that the latter substance is one of the normal precursors of epinephrine, and that when, in consequence of the destruction of the adrenals, epinephrine fails to be formed, these substances accumulate in the skin and are converted into pigment. (Quoted in A Clinical Study of Addison's Disease; Rowntree and Snell; page 173.)

(4) According to Cannon, epinephrine is responsible for the phenomena of rage. (Cannon in Barker's *Endocrinology and Metabolism.*)

From the above statements I would suggest the following scheme (it is too much like guesswork to be given the dignity of an hypothesis) for investigation: Black rats have less chromaffin tissue than grey ones. They therefore manufacture less epinephrine. As a consequence they are less savage. Also, less of the normal precursors of epinephrine will be used in its manufacture, therefore there will be more available for pigment formation. So that the rats are black. Finally, the gene which is responsible for the association of coat colour and behaviour is not pleiotropic in its action, but controls the amount of chromaffin tissue present in the body.

I would like very much to investigate this myself, but as I am at present in the navy it is not possible. However, it may come to the notice of someone who has the necessary time (and money) and interest to do so. It would be a tremendous undertaking. I know of no definite evidence for the statement that black rats have less chromaffin tissue than grey (the suggestions of Keith and Stockard are of interest in this connection), and the estimation of the total amount of this tissue present in even one rat would be quite a lengthy process. However, I would like to make one more quotation to indicate the importance of the subject, from Haldane's *New Paths in Genetics*, 1941: "in fact, the colours of animals and plants are indices of their metabolic processes, and though colours may have a protective value, this is not necessarily the basis of their selective value."

Yours faithfully,

A. J. Lea,

(Surgeon Lieutenant, R.N.V.R.)

"Four Winds"
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England

Comment by Dr. Keeler

I have always believed that there are a number of intermediary paths between the black locus or any gene locus and the correlated effects on behavior. Surgeon Lieutenant Lea has pointed out what may be one of the important paths because of the known effects of the adrenal upon both pigment development and behavior.

The work of Shophach, Keeler and Greenberg (*Growth* 7:83-95, 1943) was directed toward looking for a tie between thyroid size, behavior, and basal metabolism. We assumed that a high basal metabolic level would be found in grays because of their larger thyroids, plus greater savageness and activity. We were surprised to find actually the opposite: namely that mutants have much higher metabolic rates than do grays. The conclusion is that grays burn their fuel most efficiently as a result of natural selection in the wild (and that color mutations reduce this efficiency). So it may well be that Lea's suggestion will uncover the outstanding path, since complications have arisen with the thyroid clue that looked promising.

The approach chosen by Shophach, Keeler and Greenberg was suggested by the data given in a chart on page 245 of the paper by Keeler and King (*Jour. Comp. Psychol.* 34:241-250). This chart shows that mutant albinos, piebalds and blacks have smaller thyroids than do grays,—black thyroids being astonishingly small. Correspondingly, blacks were estimated as almost nil in savageness and wildness. That all mutations are low on voluntary exercise is shown by the chart. It also shows that thyroids, hypophyses, suprarenals and gonads of albinos are slightly smaller than "wild type." For browns all of the glands are as large as for grays, save that the gonads are reduced. For blacks most of the glands are probably reduced. For piebalds, the glands are in general reduced. For curly, a very savage group, these glands are all large.

Consequently, I felt that some of the paths must lead between the coat color gene and behavior through thyroid, suprarenal and gonads. The change in voices of mutants recorded and analysed with the collaboration of Showers and noted by Keeler and King (*ibid*) also suggested a functional alteration, possibly of the thyroid.

But there must also be paths between coat color genes and behavior that lead through the nervous system, since there is a general reduction in brain size in mutants. The chart referred to above shows paraflocculi and olfactory bulbs reduced in mutants, and my general observation is that mutants are never so disturbed by the presence of strangers as are grays. It was noted in the paper by Keeler (referred to by Lea) that albinos may be greatly deficient in the sense of smell.

I believe it highly important to support not only the research that Surgeon Lieutenant Lea has suggested, but also the complete program of exploring all the paths, anatomical and physiological, that lead between the coat color genes and behavior.

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VII

GENE DETERMINED PHYSICAL MODIFICATIONS AFFECTING THE SOCIOMETRY OF RATS

CLYDE E. KEELER

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Any explanation of individual variations in the social behavior of a mammalian species must include reference to some of the characteristics that Darwin found to distinguish wild members of a species from its tame derivatives. The following quotations will be worth our consideration in this respect:

"Complete subjugation generally depends on an animal *being social in its habits* and on receiving man as the chief of the herd or family."

"With extremely few exceptions, all animals and plants which have been long domesticated *have varied greatly*."

"It is notorious how greatly the *mental disposition, tastes, habits, consensual movements, loquacity or silence, and tone of voice have varied* and been inherited in our domesticated animals."

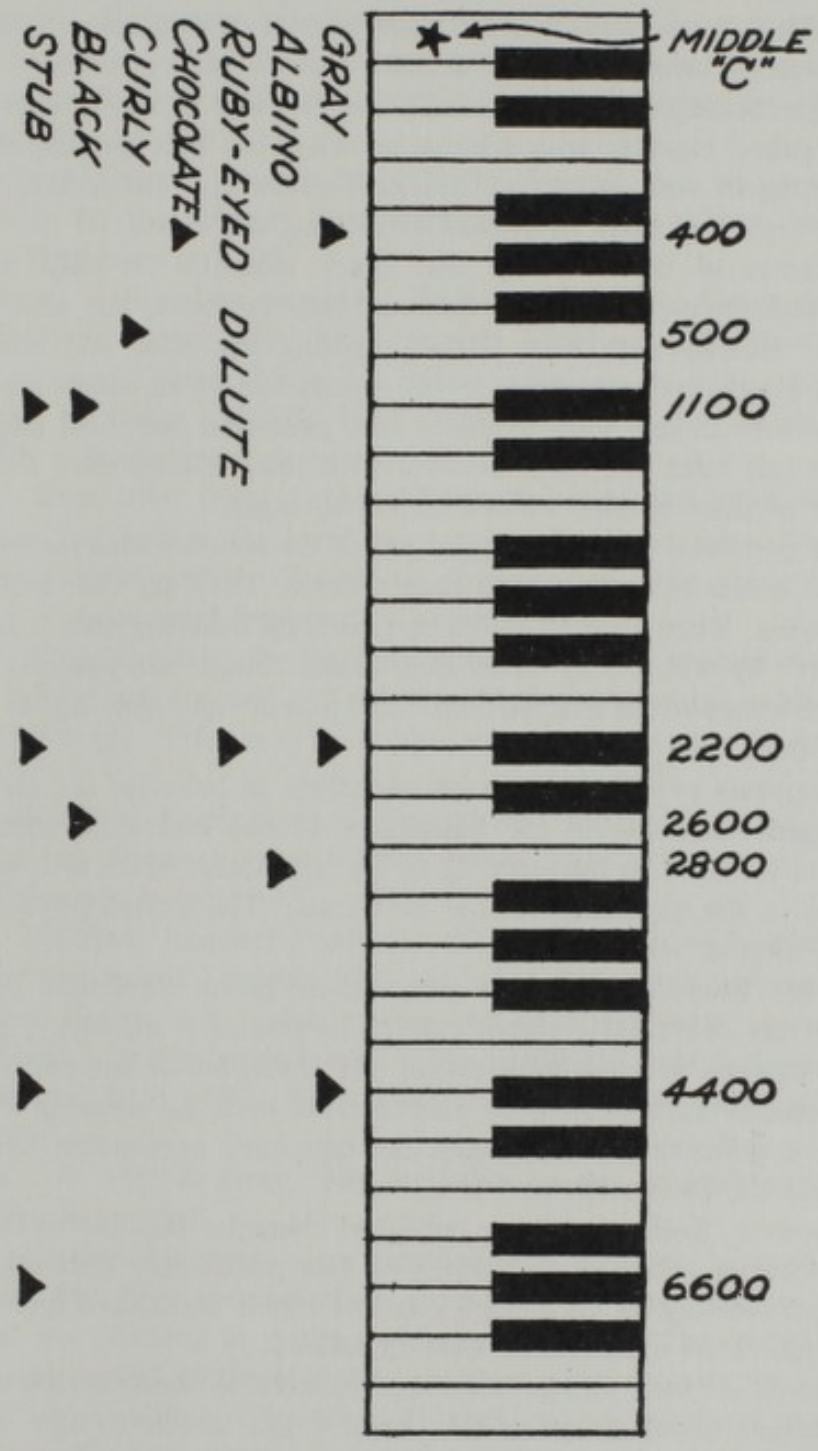
Among the reasons assigned by Darwin to account for these differences were good food and little exercise which he believed to have caused the domestic rabbit to have more than doubled the weight of the wild rabbit.

Other Darwinian alterations in the rabbit are indicated by the quotation: "The skull has increased in length but not in due proportion to the increased length of body."—"The brain has not duly increased in dimensions relative to the increase in body size or else has actually decreased."

One has only to attend a Dog Show in order to find ample evidence to prove that breeds inherit "behavior trends" with reference to particular situations. That is, individuals of two contrasted breeds tend to solve the same problem or situation in different but characteristic fashions, which behavior patterns are inherited somehow in the breed. For example, a Pointer sees a rabbit and "freezes" in silence, but a Foxhound goes after the rabbit, barking the while. A German Shepherd and a Boxer each meet an intruder. The Shepherd barks violently and flies at the man's throat. The Boxer silently topples the man over with great force and his front feet, and keeps him there quietly.

Terriers just cannot help digging, and Dalmatians that never saw a coaching performance have broken their leashes to run happily under a passing wagon. Other breeds show special tricks or talents, but little has been done toward measuring the results of these tendencies when applied to social behavior in the presence of their fellows. In a dog there is just too

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MIDDLE "C"
400
500
1100
2200
2600
2800
4400
6600
GRAY
ALBINO
RUBY-EYED DILUTE
CHOCOLATE
CURLY
BLACK
STUB

much action, personality, and too many modes of expression to be able to measure social behavior in any detailed fashion with ease.

A questioning of fanciers reveals that in most breeds of dogs the pups may be raised together with relative security, but that anti-social behavior is so strong in such breeds as Boston Terriers and Dobermans that they must be separated early to prevent mutilation and death.

Breeders of raccoons say that black mutants not only tame more readily and more permanently than do gray raccoons, but also that they are more friendly with their fellows, fighting less often and less savagely than do grays, and returning to the woods less often when given opportunity. There is also some evidence that pink-eyed buff field mice, ground squirrels and mink are more amiable with their fellows than are the gray varieties of these species when confined to cages.

The personnel of racing stables tell of the superior stamina of Dun and Chestnut horses in contests with their fellows. They say that a Black horse seldom wins. They account for these trends by believing that it is a matter of "heart" by which they mean that (other things being equal) Dun and Chestnut horses retain longest their "will to win" and that Blacks lose most quickly their "will to win."

It appears probable that such variations in behavior are the result of mutant-gene variation in the inheritance of the individual that produces structural variation in the anatomy of the individual, which in turn produces variation in the physiology of the individual. The altered physiology must produce altered behavior.

It has been customary to assign these breed differences in behavior trend to the sum-total of modifications in general morphology, gland, and nervous system, which is undoubtedly the truth, but it has not been generally conceded that single-gene substitutions such as those producing the coat color differences of the fancy can determine measurable trends in, or syndromes of, personality and behavior.

However, Keeler and King published character sketches of the idiosyncratic behavior exhibited by strains of rats presumably differing from the wild Gray Norway in but a single coat color gene and reared under identical conditions. Their descriptions were as follows:

Mutant Albino. Cringe when approached after being completely tamed, When tamed, about as apt as the tamed Grays to bite or fight back when picked up. When not tamed, as wild and vicious as the Grays. When dropped on the floor they attack the caretakers as Grays do. It may be added that instead of running to the attack, they usually advance by a

series of bounds. Voice may be a high, sustained whistle having fundamental tone at a frequency of 2800 cycles per second and having no overtones, whereas the rough, loud Gray voice may have a fundamental at 400 with overtones at 220 and 4400.

Ruby-Eyed Dilute. Known to be fairly sluggish, but was not available for study on the original Gray background. Voice a high sustained tone with a frequency of 2200.

Cinnamon. (Chocolate pigment) Easier to tame than Grays, but may revert to the wild nature after being tamed. Vigorous and active. Ordinarily more peaceful than Grays, but when called on to fight, they fight quite as well as Grays. Rough, loud voice similar to that of the Gray Norway with a fundamental frequency at 400.

Curly. Even after being tamed difficult to catch, but when removed from the cage and held in the hand, they ordinarily do not bite. They can never be completely trusted. Voice: low, unsustained, with many varying components. Fundamental frequency is about 500.

Black. Sluggish. Already tame by nature. If very excited they may click their teeth, but are not apt to bite. Many only whine softly when picked up with tongs. Voice may be a high, sustained tone with fundamental at 1100.

Albino-Waltzer. Easier to tame than mutant Albinos from which they were derived but always nervous. When tamed, they seldom turn on the observer. Voice not tested.

Stub. Dwarfed, frequently tailless. Always fighting each other. Go out of their way to pick trouble. Do not mind their own business as do gray rats, but throw their bodies against the cage wire when anyone approaches. Voice is a high squeak with great amplitude at high frequencies. The fundamental is at 1100. Both 2200 and 4400 predominate with the peak at 6600.

Piebald. As wild as Gray. Not available on the original gray background. Voice not tested.

These behavior differences were recorded with reference to their handling by man, but they show distinct alterations in temperament and in abilities that are involved in dealing with their fellows. The modifications of response discovered in these studies show us what to look for in their interpersonal relationships. The physical modifications of these rats that are correlated with their altered behavior will apprize us of what sorts of physical modifications are important as determiners of observable variations in the interpersonal relationships of rats in particular. And for any other

species of mammals these physical characteristics play a similar role in determining behavior trends.

Body Size

Ordinarily among rats, the largest and strongest male in the cage rules his fellows with violence and, whether or not they fight back, the lesser males usually have their pelts covered with bites. The females ordinarily do not challenge the authority of the "big brute", but, nevertheless, he may give them an occasional nip just to keep them "thinking right".

Among rats there is a strong sense of possession that develops the individual morale, and a lesser male that has had a cage of his own will fight like a demon to defend it if the "big brute" is inserted into his cage. The sense of possession is also found in females, and in some cases it is dangerous to the life of the "big brute" male who apparently recognizes this right of ownership, because he seldom fights back with his usual savageness when placed in a strange cage that is being defended by either a lesser male or a female claimant.

Accordingly, I have seen seven males that were castrated or killed outright consecutively by a virago that resented their intrusion into her cage.

On one occasion a female, living alone, violently attacked a certain male every time that he was put into her cage. She was shifted to a new cage, but this did not reduce her antagonism appreciably. As a last resort, the male was etherized and placed in her cage "dead drunk". The female appeared bewildered by his unusual odor and staggering movements, and she made no attempt to attack him. On the contrary, when he gradually "came to" she accepted him fully as her cagemate and consort.

In all such contests body size plays a highly important role, other things being equal. It is now well known that some coat color genes make for larger and some for smaller bodies than the average.

Some coat color variations such as Chocolate pigment and Curly coat produce a greater length than normal, correlated with a corresponding increase in weight. Other genes, such as Hooded, Albino and Ruby-Eyed Dilute, decrease correspondingly both in length and weight. The Waltzing gene decreases length, but does not change weight, thus altering the bodily proportions completely. In two-gene combinations the effects of the genes are additive, observing the plus and minus signs. That is, the possession of two genes each inducing greater than average size will produce an animal still larger than if it possessed but one of these size-increasing mutant loci. Likewise, the possession of two gene mutations, each inducing smaller than

average size will produce an animal still smaller than if it possessed but one of these size-reducing mutant loci. And lastly, an individual, having received a growth increasing gene and a growth reducing gene, will be of average size, the two contrary tendencies having cancelled each other out.

Various coat color genes lengthen the tail slightly, and probably make it much thinner than normal, which modification would be a distinct disadvantage as a support in fighting.

General Physiology

In all of their bodily processes, it appears probable that most mutants are physiologically older than wild Gray rats of the same chronological age. That is, mutants in general seem to spin through their life processes at a faster rate than do wild Grays. If this be true, this fact might seem to throw a small advantage to the mutants during early months, but when the wild Gray rat is in its prime, a mutant of equal chronological age will have started to decline, and this fact should be and is detectable in such a general character as loss of water content in bones and tissues and possibly in a corresponding reduction in general strength. The relative rates of natural drying for different parts of the body will normally follow an axial gradient, the form of which is altered in some mutants, and the altered axial gradient, we may suppose, will have a slight effect on the bodily distribution of strength in an individual.

Acuity of Vision

Such coat color variations as Pink-Eyed Dilute, Red-Eyed Dilute, Ruby-Eyed Dilute or any other genetic entity that reduces or increases interocular pigmentation, of necessity put the bearer at a disadvantage in interpreting his surroundings, including the actions of his fellows and, accordingly, he is likely to be less certain of himself and less on his guard. The flashing of images vividly upon the Albino retina, for example, may actually keep an individual in a constant state of bewilderment.

Hearing

Although we do not have measurements of the dulling effects of mutant coat color genes upon auditory response, we may be certain that such exist and are of measurable size, because rats bearing coat color mutations are less sensitive to high-pitched sounds than are wild Gray rats maintained in the same laboratory.

Olfactory Sense

Important as eyes and ears may be in evaluating the environment, they are of not nearly so great importance as is the sense of smell in rats. Correspondingly, the deficiency variations in the olfactory sense will be of much greater importance to interpersonal behavior. It is the sense of smell that keeps the wild Gray rat most alert for danger and for the challenges of his fellow rats or other enemies. If both wild Grays and mutants are kept in the same laboratory the Grays immediately sense the presence of a human stranger as much as 40 feet away, whereas the mutants seldom pay any attention to him until he stands before their cage. Furthermore, it takes two weeks for wild Gray rats to get used to a new caretaker, whereas the mutants mind the change very little.

Evidence was obtained that would indicate that a greatly reduced sense of smell may accompany the Albino gene in rats, and a strain of laboratory Albinos (latently purebred for Hooded and Black) was found to be completely insensitive to the smell of garlic that all other rats hate. Evidence was also collected that showed these Albinos unable to smell the garlic, but that they could taste it, hating the taste as other rats do.

The impairment or loss of the sense of smell by a rat would be something like the impairment or loss of vision would be to a human being, and it certainly does affect interpersonal relationships to a great degree, putting these creatures to a great disadvantage before their fellows as well as exposing them to other dangers of the environment.

Touch

We have no evidence upon the sense of touch in rats, but an observation drawn from mice would seem to indicate that an unusual coat texture or absence of hair may be acted upon by other rats in their interpersonal relationships. A litter of half grown mice included two hairless ones. A new litter was born in the cage and for a number of days two females made life miserable for the hairless members of the older litter by trying to drag them constantly into the nest with the naked newborns.

This curious interpersonal reaction on the part of the females would appear to be due to the lack of hair on the half grown mice being confused through the sense of touch with the lack of hair on newborns.

It may be suggested that some mendelian genes, as that for Hairless, may produce skins that are dulled in the sense of feeling, and in cases in which ulcers are present, an even more sensitive skin such as found in old Hairless rats. Both of these conditions will undoubtedly affect interpersonal relationships as preliminary observations have shown,

Quality of Voice

Because rats are more disturbed by sounds at high frequencies than at low frequencies, it would appear that voice modification may play an important role among rats in dealing with their fellows and in giving alarm.

The variations in voices of rats have been recorded and analyzed for a few adult males of several coat color strains as well as for wild Gray controls. The general voice characteristics have been given above for several strains. A summary of principal frequencies involved in these analyses is shown in the accompanying illustration that represents the upper half of a piano keyboard beginning with Middle "C". The frequencies indicated above the keyboard are given in cycles per second, assuming that the piano is tuned to "perfect pitch". The frequencies found in the voices of various rats are indicated by wedges placed directly below the key to which these frequencies correspond. Some very curious facts were uncovered by this study that probably affect interpersonal relationships. In general, the voices of mutants are raised in frequency of the fundamental, but this is done almost invariably with greatly reduced volume. There seems to be no modulation of voices by voluntary changes in shape of the voice apparatus, but all rats appear to raise their voices to higher and higher frequencies by sending air through the apparatus under greater pressure, so that the pitch of voice continues to mount higher and higher as additional multiples of the fundamental frequency are produced. The fundamentals of voices of mutants analyzed were raised with the exceptions of Curly Coated and Chocolate Pigmented rats, whose fundamentals remain similar to those of wild Gray rats. The Albino gene alone tends to change the general pattern of the voice as well as the position of the fundamental. When this gene was placed upon a wild Gray background, the animals tested developed voices with almost a pure single frequency of 2800 cycles per second, the quality of this voice sounding much more like a flute or whistle than a squeal.

Because a predominance of powerful tones at high frequencies gives to an individual rat a voice that sends terror into his fellows, any coat color, bringing with it a reduced volume, even though the fundamental is raised, will be of disadvantage, because wild Grays can and do produce more powerful voices at higher and higher frequencies merely by forcing air through the normal voice box under greater pressure.

Glands

Greater docility, lack of savageness and the taking of less exercise would be expected to reflect some glandular alterations, and correspondingly

evidence that the thyroids, adrenals and testes were reduced in most mutants was found in the dissection records of the late Dr. Henry H. Donaldson. These data were published by Keeler and King in summary.

A reduction of activity would put a rat at disadvantage in interpersonal relationships and would be expected to stem from some basal metabolic change. Schopbach, Keeler and Greenberg found that the Black metabolic rate was above that of the wild Gray but suggested that the Black rat burns its fuel with comparatively low efficiency. The heart rate was found to be increased slightly in Black mutants.

The lack of aggressiveness in coat color mutants with high voice fundamentals appears to be related to the reduced size of their testicles. The testicles of both Curly and Chocolate rats are of about normal size, their voices have fundamentals about as low as those of wild Grays, and they are aggressive fighters.

Because in the studies of Schopbach, Keeler and Greenberg hypothyroidism was ruled out as the cause of docility and tameness in the Black rat it is tentatively suggested that these characteristics are dependent upon a reduction of adrenal function. This possibility remains to be studied.

Muscle Tonus

No studies have been made upon the subject of muscle tonus; suffice it to say that the handling of the different breeds both alive and as carcasses gives one the distinct impression that the muscles of mutants in general are softer and flabbier than are those of wild Gray Norway rats. If this strong impression is proven by actual tonus tests, this fact is also to the disadvantage of the mutants in general.

Discussion

It would seem probable that much of the physical basis underlying differences in interpersonal behavior between wild Gray rats and their mutant coat color derivatives are due to the clipping off by the coat color genes of bits of the organism (by faulty development) here and there, in sense organs, brain, glands, size, general strength, voice and possibly other ways. To put it crudely, the laboratory mutant has so much of itself excised that it is really no longer a rat when compared with the unmutated members of its species. And because it is not a rat, it cannot be expected to behave as one.

These genes induce modifications similar to Darwin's "effects of domestication".

If we try to apply the findings of these studies to problems of interpersonal relationships in man, we must admit at once that, in general, the little push that a single gene makes in one direction or another on trends of behavior is so swamped, or modified or voted down in man by the thousands of other genes in the residual hereditary background of the individual that it would be extremely difficult to evaluate its specific effects or apply them to particular situations in behavior. However, in rats studied in the laboratory, by making identical the residual hereditary backgrounds for all individuals, the effects of particular allel-pair alternatives displayed upon the identical backgrounds will stand out clearly.

It is apparent, however, that the types of physical and physiological modification that we have shown to be brought about in the rat as pleiotropic manifestations of single genes that lead to altered trends in interpersonal behavior, actually have their counterparts in man and do affect his behavior in relation to his fellows, although less obviously.

It seems probable that the sense of smell plays an important role among primitive peoples who depend upon that sense more in their adjustments than do more civilized peoples, and yet the large perfume trade of the world is based upon the great extent to which odor still affects the daily lives of civilized peoples. Tea, coffee, tobacco and food trades are also affected. I have heard a European woman complain that she hated one of her grandchildren "because he does not smell like our people", and it is well known that strong and generally repulsive bodily odors are definitely inherited in families of cleanly habits. Persons so afflicted by bodily odors find it impossible to hold positions of refinement.

In those days when success depended more upon the ability of the individual in physical contests, the matters of body length and body weight played an important role. And, although reduced in value today, these factors are not without their influence in human affairs because, other things being equal, the tall, well-built man is preferred as a leader.

In the matter of voice, no one will deny the magnetism of the silver-tongued orator. Ask members of his audience what he spoke about and they will reply, "I really don't know what he said, but I remember that he had such a wonderful voice." Success in several professions of leadership and influence such as movies, radio, politics and the ministry are often bound up with the possession of a pleasing or effective voice.

We have mentioned modification of the glands that determine temperament changes to a great extent in rats: the thin, hyperthyroid, vicious Curlys and the friendly, plump, sluggish Blacks. It is a commonplace to

speak of the thin, hyperthyroid, human-dynamo type of man with his activity and drive in contrast to the fat, baldish, hypothyroid, affable wheel-horse that carries out directions faithfully.

Possibly the additional stimulus to brain desiccation induced by certain genes may affect human reactions to a certain extent as yet unmeasurable. We do know that early maturity of mind in a person is looked up to in youth, but the same individual will be forsaken as a leader in middle life should he begin to exhibit sluggishness of mental reaction that may conceivably accrue from accelerated cerebral desiccation.

It has been shown that a number of the factors we have examined in the rat and that we have demonstrated to be due to the pleiotropic effects of simply inherited genes also affecting hair form and pigmentation, do change interpersonal behavior in the Norway rat. We have noted that most of these same variations may modify interpersonal relationships in man, although here their influences are still subtle and defy exact evaluation.

It will be seen that in rats the possession of certain gene mutations in general, places a rat at a disadvantage before his fellows with regard to his interpersonal relationships through the general weakening of his body, the dulling of his sense organs and the calming of his reactions.

If an accumulation of mutant genes produces similar physical and physiological effects in man, and it seems probable that this is the case, then it may not be to the disadvantage of the possessor of these traits in dealing with his fellows in a world built on heterogeneity of capacity and ability. Calm and cool-headed persons, rather than kinetic, impulsive or explosive ones, usually serve us well in capacities of trust and judgment such as bankers and judges, who bear the confidence and respect of their fellow citizens.

Some day we may even find that such a dulling of the sense organs that tempers and to a certain extent shuts out stimuli and threats of the environment, a weakening of the body that destines man to construct with tools rather than do everything with his muscles, and a calming of his mental tempo that gives him time to think and plan, to tolerate others, and even to consider the welfare of his community as a whole (rather than to quickly hide, run or fight in response to disturbing stimuli), were important factors in bringing about the development of human civilizations in which millions of individuals live as basic units in a beneficial interpersonal relationship and socio-cultural unity. It is obvious that a colony of such unlimited size has been achieved by no other mammal, and we may owe this to an accumulation of just such behavior modifying genes as we have studied in the rat.

Summary

To summarize the foregoing argument, we may say that we believe that most of the behavior trends observed in coat color mutants having a common, residual hereditary background can be explained as due to several types of pleiotropic modification accompanying the presence of the coat color genes themselves affecting glands, nervous system, etc., namely, the genes for Chocolate, Curly, Hooded, Albino, Ruby-Eyed Dilute, and Waltzer. The effects are similar to those that Darwin thought due to the domesticative environment. These alterations are of the same nature as Darwin's modifications due to domesticative evolution.

It is suggested that valuable progress will be achieved in the experimental study of interpersonal relationships in rats when animals of identical residual hereditary background and bearing single coat-color-gene-induced behavior trends as well as animals bearing more complicated combinations of diverse single-gene trends can be raised to adulthood without handling with their own genetic type and then brought together with other individuals bearing similarly synthesized but diverse personalities so that the interpersonal reactions of different combinations may be observed, recorded and analyzed.

Whereas in man the measurement and evaluation of the effects of such variations upon interpersonal behavior is extremely difficult, we have shown that just such variations in build, glands and nervous system do affect materially the interpersonal reactions of human beings. These same factors may have had something to do with the development of civilizations.

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VIII

LES EFFETS DES VARIATIONS DU POIL SUR LA MORPHOLOGIE, LA PHYSIOLOGIE ET LA CONDUITE DU RAT NORVEGIEN

PAR

Clyde E. KEELER

Des analyses récentes ont amené à la conclusion que les facteurs génétiques qui produisent les caractères du poil peuvent être considérés comme des indicateurs colorimétriques ou morphométriques extérieurs des myriades des processus physiologiques variables qui procèdent continuellement dans toutes les parties de l'organisme.

C'est-à-dire que le plan de l'organisme qui possède le caractère de poil mutant est modifié partout, en produisant des organes un peu différents en taille ou en qualité quand on les compare avec les standards du rat norvégien sauvage, et la physiologie modifiée de ces organes, avec leurs interactions et contre-actions, intègre l'or-

BULL. SOC. ZOOL. FRANCE. LXX. 1945. pp. 123-124.

ganisme total d'une façon unique pour chaque facteur génétique qu'on a examiné.

Nous ne pouvons plus envisager l'étude de la couleur du poil chez les Mammifères comme un but génétique, de la manière dont on l'a traitée pendant beaucoup d'années, mais il faut la regarder comme une méthode pour l'exploration de tout le royaume de la physiologie de l'animal.

Les endroits favorisés par les modifications sont : taille générale du corps, queue, testicules, fémurs, bulbes olfactifs, os nasaux. Les facteurs génétiques qui produisent ces modifications du poil peuvent affecter le poids de la cervelle entière, la vitesse de la perte naturelle de l'eau dans les os et dans la cervelle, peut-être la grandeur et la forme du *foramen magnum*, l'activité générale, la docilité, la nervosité, le métabolisme basal, la vitesse du cœur, les caractéristiques de la voix, le poids du corps entier, l'habitude de ronger le bois, la quantité de nourriture prise, le choix du régime, et la solidité des muscles. Plusieurs modifications anatomiques sont limitées par le sexe, comme la queue courte chez les femelle « Cinnamon » et « Curly », les os nasaux courts chez les mâles de la race « Cinnamon », et le fémur court des mâles de la race « Curly ».

Ainsi la couleur unique du poil de l'animal mutant, par exemple, est comme un billet ou une liste affichés à l'extérieur de l'individu indiquant exactement au physiologiste ce qu'il va trouver à l'intérieur.

On a publié quelques preuves de cette conclusion dans la liste ci-dessous, et on en publiera plus tard le reste.

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IX

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THE EFFECT UPON ULTIMATE BODY SIZE PRODUCED BY COMBINING CERTAIN COAT-CHARACTER GENES IN THE NORWAY RAT[1]

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Introduction

A general summary of earlier work of the author on this problem was read before the American Society of Zoologists at Dallas, Texas, in 1941 and published with additions later (Keeler-King, 1941-1942). These general papers showed that many measurable modifications in morphology, physiology, and behavior were correlated with the presence of certain coat-color genes. Special attention was given to variations in body size, dependent upon the coat-color genes: albino, black, and piebald, which distinguish the Wistar albino rat genetically from the gray Norway rat.

In the above paper, emphasis was placed upon the extremely "domesticating effect" associated with the black (non-agouti) gene, and further observations[2] on this effect have demonstrated that it is capable of neutralizing even the relatively "wilding effects" of the genes for curly, piebald, and albino. The chart shown at the Dallas meeting compared a series of modification profiles for various coat character strains of rats, of which albino, cinnamon (brown), piebald (hooded), black, ruby-eyed dilute, and curly were direct mutants from the gray Norway strain mentioned. These modification profiles were based on average measurements such as those of general body size, skull dimensions, organ weights, and other anatomical proportions, together with records of behavior. Where the average age of the mutants showed that they represented adults that had virtually received their full growth (300-600 days), a number of significant differences were at once apparent. Among these was a tendency to general reduction in size of various endocrine glands, which fact was

[1]This paper presents an analysis made and written in 1941 at the Wistar Institute by the author while he held the titles of Fellow and Curator of the Experimental Colony. It was presented to the Board of Scientific Advisors in the spring of 1942 and was read before the Georgia Academy of Science in April, 1946.

[2]The differences in response of grays and blacks to several behavior situations were examined statistically by the author (Keeler, 1942, 1945) and a number of these differences were found to be significant. Shopback, Keeler, and Greenberg (1943), working at the Lankenau Hospital, explored the physiological modifications of basal metabolism and heart rate. These metabolic and heart rate findings are related to the problem of body size because body size, body proportions, and metabolism are to a large extent the result of the relative size and efficiency of the endocrine glands, which are also important factors in modifying behavior.

undoubtedly known to the late Dr. Henry H. Donaldson, although unpublished.

Of course, the mere pictorial representation of characters for various mutant strains as compared with their gray Norway relatives are unsatisfactory. Each of the measurements in the Keeler-King charts should be examined, controlling, in as far as possible, environment (quarters, food, care, etc.), individual age, and individual body length. All anatomical characters of the rat may vary enormously with these factors. Indeed, because of the great variation in length of rats that have practically reached full growth, and because of the close correlation of organ size with body length, most of the anatomical data ought not to be studied statistically without first making corrections for individual variations in body length. However, it is admitted that many of the variations are gross enough to be detected without such corrections and that a number of these are recognizable as statistically significant in the Dallas chart.

There is one exception to the desirability of correction for length, and that is with regard to measuring the total growth impetus which is expressed in general body weight. For the study of this phenomenon, animals corrected for age but not for length must be employed.

The charts of the Dallas paper indicated definitely that effects accompanying coat-color genes modify body size. In fact, it was shown that by adding together the qualitative modifications of morphology and behavior produced by the three genes (black, piebald, and albinism), it is possible to account for most of the differences between the wild, gray Norway rat and the tame laboratory albinos studied by Donaldson. The physical modifications of the laboratory albino had been attributed previously to the "effects of domestication" by Donaldson (1906), Watson (1907), and others: Body size was one of Darwin's "marks of domestication." This genetic explanation of the so-called effects of "domesticative evolution" assumed that plus and minus trends associated with various coat-character genes were to a certain extent additive. One purpose of this paper is to examine and discuss in detail the additive interaction of growth tendencies affecting body size, which tendencies are associated with coat characters in the Norway rat.

Previous Observations

That coat-color genes may affect general body size in rodents has been demonstrated for mice by Feldman (1935), Green (1931), Castle and his collaborators (1936), and hence we may expect some genes to increase body size, others to decrease it. That the effects of unit-gene action may be additive regarding plus and minus signs has been shown in one case by Castle *et alii* (1936), in which the increaser-effect of blue-dilution was negated by the decreaser-effect of short ears in house mice.

Materials

The raw data of this analysis consisted of dissection records made by Miss Ruth Meeser, research assistant to the late Dr. Henry H. Donaldson, for his investigation into "the inheritance of acquired characters" that was left uncompleted at his death in January, 1938. The gray Norway and mutant rats used were raised by Dr. Helen D. King, who, after she had discarded them from her experiments and had killed them, turned their corpses over to Dr. Donaldson for his studies.

Specifically, the author proposes to study statistically the relations between the weights and lengths of rats and various coat and other characters. The following statistical relations will be considered for each sex: mean, standard error of mean, standard deviation about mean, difference between means, and probability of difference between means being due to errors of random sampling.

Test for Significance of Differences

Unless otherwise mentioned, all differences between mean values compared in this paper are considered to be statistically significant. By this is meant that the probabilities of the means of the two samples being compared actually representing the same statistical population is less than .05. For population samples of the size here employed the probabilities corresponding to differences in values of t (Fisher's chi-square method) are given herewith.

In the subsequent tables there is given the standard error for differences between the means as well as the values for t. In the tables and charts the differences between means that are not significant are marked with an asterisk.

	Considered significant									Considered insignificant			
Probability	.9	.8	.7	.6	.5	.4	.3	.2	.1	.05	.02	.01	.001
	.126	.253	.385	.524	.674	.842	1.036	1.282	1.645	1.960	2.326	2.576	3.291

Controls

Because the mutants arose between the 12th and 21st generations of the gray Norway stock (some mutant individuals were not isolated until several generations later), measurements of the gray Norway rats (307 males and 304 females) were chosen from these generations as an environmental control as well as a control of the residual hereditary background. Earlier and later generations of gray Nor-

way rats were not used as controls because of proportion and size "drifts" that may take place in strains, probably due to further mutations and their tendency to become homozygous upon strain inbreeding which occurs to a certain extent under all ordinary laboratory breeding procedures.

Results

The results of this study have been recorded in three tables and six charts. Table 1 is a comparison of mean weights of male and female populations of cinnamon, curly, hooded, curly R.E.D., curly hooded, albino waltzer, and albino rats with appropriate control populations of gray Norway rats. Table 2 is a comparison of these same strains of rats for body length. Table 3 is a comparison of the mean weights and of the various mutant strains with each other, table 4 is a comparison of mean lengths of the various mutant strains with each other. From the data in these tables the charts were prepared. The charts demonstrate the primary growth effects of the various mutant coat-character genes as well as their resultant interactions when several mutant genes are combined in the same individuals. The charts will be described in detail in the text.

Body Weight. Records have been examined for a number of strains of mutants having the same gray Norway residual hereditary background. The controls consisted of gray Norway adult rats: 307 males having a mean body weight of 434.62 gm. with a standard error of ± 1.78 gm. and 304 females having a mean body weight of 338.17 gm. with a standard error of ± 1.48 gm. Sixty cinnamon male rats exceeded the male controls in weight with a mean of 457.73 ± 1.69 gm. The difference between the means of the control males and the cinnamon males is 23.11 gm. The difference between the means of the control females and the cinnamon females is 13.87 gm. Seventy-six curly males exceeded their controls with a mean weight of 473.01 ± 3.98 gm. Eighty-four curly females exceeded their controls with 342.84 ± 2.25 gm. The difference between the means for curly males and control males is 38.39 gm. The difference between the means for curly females and control females is 4.67 gm. This latter deviation is not statistically significant, suggesting that possibly sex factors may modify the behavior of the curly gene. However, employing as controls the group of gray Norway rats employed in the Dallas chart (from 1st to 35th generations), body weight of curly females is shown to be larger than that of their controls, and hence we can draw no definite conclusion as to sex-limited behavior. Seventeen hooded (piebald) males are inferior to their controls with a mean weight of 411.94 ± 5.75 gm., and 19 hooded females are inferior to their controls with a mean weight of 295.74 ± 0.94 gm. The difference between the mean weight of the hooded males and their controls is 22.68 gm. The difference between the mean weight of hooded females and their controls is 42.43 gm.

One hundred and thirty-nine albino males were inferior to their controls with a mean weight of 396.82 ± 2.42 gm. whereas 124 cor-

TABLE 1. *A comparison of average weights of mutant rats with the average weights of their gray Norway controls*

Strain	Sex	N	Mean Weight In Grams	Standard Error of Mean	Standard Deviation About Mean	Difference Between Means	Standard Error of Difference Between Means	Values of t	Probability That the Difference Between Means is Significant
Gray.....	Male	307	434.62	1.777	31.09	.....	.....	.....	.....
Gray.....	Female	304	338.17	1.476	25.70	.....	.....	.....	.....
Cinnamon.....	Male	60	457.73	2.781	21.36	23.11	29.7904	5.4958	Less than .001
Cinnamon.....	Female	69	352.04	1.688	13.92	13.87	23.9595	4.3411	Less than .001
Curly.....	Male	76	473.01	3.982	33.71	38.39	31.7022	9.6954	Less than .001
Curly*.....	Female	84	342.84	2.250	20.50	4.67	24.7312	1.5319	Less than .200
Hooded.....	Male	17	411.94	5.745	22.98	22.68	30.8014	2.9553	Less than .010
Hooded.....	Female	19	295.74	0.943	4.00	42.43	25.0291	7.1696	Less than .001
Curly R.E.D...	Male	37	448.24	5.531	33.19	13.62	31.4033	2.5257	Less than .020
Curly R.E.D...	Female	34	327.56	2.124	12.20	10.62	24.7607	2.3718	Less than .020
Curly Hooded*	Male	14	430.57	7.689	27.72	4.05	31.0379	0.2357	Greater than .900
Curly Hooded*	Female	8	320.75	14.981	39.64	17.42	26.2346	1.8538	Greater than .100
Alb.Waltzer...	Male	16	416.25	7.777	30.12	18.37	31.1297	2.3013	Less than .050
Alb.Waltzer...	Female	17	313.82	5.128	20.51	24.35	25.5313	2.8267	Less than .001
Albino.....	Male	139	396.82	2.416	29.38	37.80	30.6330	12.0700	Less than .001
Albino.....	Female	124	305.21	1.157	12.83	32.86	25.7865	11.9955	Less than .001

*The significance of the differences between the means in these cases is uncertain.

responding albino females were inferior to their controls with a weight of 305.21 ± 1.16 gm.

Aside from the strains mentioned which were marked by one coat-character gene, there were several others exhibiting two coat-characters apiece. Thirty-seven curly-ruby-eyed dilute (R.E.D.) males exceeded their controls with a 448.24 ± 5.53 gm. mean, whereas 34 corresponding females were inferior to their controls with a mean of 327.56 ± 2.12 gm. The difference between the means for females was 10.62 gm., that for the males, 13.62 gm. Fourteen curly hooded males were slightly inferior to their controls with a mean of 430.57 ± 7.69 gm. This difference of 4.05 gm. is not significant. Eight corresponding curly hooded females are inferior to their controls with a mean of 320.75 ± 14.98 gm. The difference between the means is 17.42 gm. The difference is not significant. Sixteen albino waltzer males are inferior to their controls with a mean of 416.25 ± 7.78 gm. The difference between the means is 18.37 gm. Seventeen corresponding females are inferior to their controls with a mean of 313.82 ± 5.13 gm. The difference between the means is 24.35 gm. There was noted a size drift downward with succeeding generations in mutant albinos, and so the first generation was examined to see if the difference between gray Norway and mutant albino is due to that drift alone. In the F_o and F_1 generations together there were 80 males and 75 females. The males had a mean weight of 416.75 gm. and the females had a mean weight of 313.67 gm. The male mean is 17.87 gm. below that of the controls and the female mean is 24.50 gm. below that of the controls.

Thus, it will be seen that we are dealing in weight with:

A. Growth-increaser effects associated with:
   1. Cinnamon in male
   2. Cinnamon in female
   3. Curly in male
   4. (Possibly curly in female)

B. Growth-reducer effects associated with:
   1. Hooded in male
   2. Hooded in female
   3. Albino in male
   4. Albino in female

An examination of the cases in which two genes are simultaneously homozygous in experimental populations, namely, in curly R.E.D., curly hooded and albino waltzer strains shows (Chart 1) that ruby-eyed dilute is associated with a decreaser effect both in males and in females. For gray males the mean weight is 434.62 gm. In addition the curly gene increases weight to 473.01 gm., but the addition of the R.E.D. gene to curly reduces the mean weight again to 448.24 gm. Similarly, gray Norway females have a mean weight of 338.17 gm. The curly gene increases this to 342.84 gm., an amount statistically insignificant. The R.E.D. gene added to the curly gene reduces mean weight to 327.56 gm. which is significantly lower than

the gray Norway mean. Thus, the plus effect of the curly gene is more than half neutralized by the minus effect of R.E.D. in males and more than neutralized in females.

The reducer gene, hooded, also counteracts the increaser effects of the curly gene (Chart 2). We start with gray Norway rats having a mean weight of 434.62 gm. The addition of hooded alone reduces the mean weight to 411.94 gm. The addition of curly alone increases mean weight to 473.01 gm. The insertion simultaneously into the genetic constitution of both curly and hooded genes homozygously results in animals of 430.57 gm. mean, almost identically the same weight as the gray Norway. Here the increaser effects of curly have been completely negated by the decreaser effects of hooded in males. A similar result is obtained from corresponding females. Gray females have a mean weight of 338.17 gm. The addition of hooded reduces it to 295.74 gm. The addition of curly increases it to 342.84 gm. But if both curly and hooded are introduced into females simultaneously, they tend to neutralize each other's effects so that in the resulting animals the mean weight is 320.75 gm, which is actually lower than, but not statistically different from, the mean of gray Norway females.

In Chart 3 the effects of albino and waltzer[3] are seen. Starting with a gray Norway male mean of 434.62 gm., the addition of the albino gene reduces it to 396.82 gm. If we combine the albino gene with the waltzer gene, the weight is 416.25 gm., which is statistically not distinct from the effect produced by the albino gene alone. A similar result is observed among females. Starting with the gray female mean of 338.17 gm., the albino gene reduces this to 305.21 gm. The addition of the waltzer gene to the albino alters this result very little, leaving the mean 313.82 gm. which is not statistically different from the albino mean.

These effects of coat-character genes on body weight may be listed as follows:

A. *Weight increasing effects associated with:*
   1. Cinnamon in male and female
   2. Curly in male (possibly in female)

B. *Weight decreasing effects associated with:*
   1. Hooded in male and female
   2. Albino in male and female
   3. Ruby-eyed dilute in male and female (known by its effect on curly)

C. *No weight effects associated with:*
   1. Waltzer in male and female.

Body Length. Table 2 shows greater uniformity within the various populations than was the case of weight as measured by the

[3]So far as is known to the author, waltzer produces no coat-character manifestation. Because of the greater facility of expression, the whole group of Mendelian characters in this study are referred to as coat-characters, although the reader will realize that waltzer is an exception to this classification.

standard deviation of the mean (Table 1). In fact, there is no exception to this rule. Such greater uniformity is to be expected because weight fluctuates much with the condition of fat storage (especially in old age), with temporary nutrition, and with temporary health conditions.

If the same factors producing increased weight are general for body size and not merely related to fat production, then increased weight is a correlate of body length due to an increase in size of possibly many or all bodily parts. However, such fat-producing genes as silver and lethal yellow are known in mice and hence we would not be surprised to find them here as exceptions.

From the general line of reasoning given above we would expect cinnamon rats, both males and females, to be significantly longer than gray Norway rats. We would also expect curly males to be longer than gray males, but we might expect curly females to be very little modified in length, although possibly to a slight extent in the plus direction. We ought to find hooded, albino, and waltzer to be genes that shorten body length, both in males and in females. The effect of hooded and R.E.D. in cancelling the lengthening effect of curly ought to be visible in curly-hooded and curly-R.E.D. rats. The effects of waltzer in augmenting the shortening effects of the albino gene should be seen in albino-waltzers.

Curiously enough, all these predictions have been fulfilled as an examination of Table 2 will show. In this table it will be seen that the 307 male gray Norway rats employed as controls had a mean length of 245.53 mm. with a standard error of 0.30 mm. The 304 corresponding female controls had a mean length of 228.36 mm. with a standard error of 0.31 mm. The 65 cinnamon males and the 76 cinnamon females exceeded their controls. The cinnamon male mean length was 248.96 $\pm$ 0.44 mm. The difference between the cinnamon male mean length and the mean length of the male controls was 3.43 mm. The difference between the cinnamon female mean length of 231.11 $\pm$ 0.34 mm. and their control mean length was 3.75 mm. The 76 curly males and the 84 curly females exceeded their controls for length. The curly male mean of 248.31 $\pm$ 0.43 mm. differed from the control mean by 2.78 mm. Although curly females exceeded their controls for length, the amount is not statistically significant (as in the corresponding case of weight). In the present case, the curly mean is 228.79 $\pm$ 0.45 mm., merely 0.43 mm. above its standard. The 17 hooded males and the 19 hooded females are inferior to their controls with mean length values of 238.05 $\pm$ 1.43 mm. and 222.21 $\pm$ 0.38 mm., respectively. The males were below their controls by 7.48 mm. The females were below their controls by 6.15 mm. The 139 albino males and the 124 albino females were below their controls with means of 239.30 $\pm$ 0.54 mm., and 223.37 $\pm$ 0.37 mm., respectively. The difference for males is 6.23 mm. and for females is 4.99 mm.

TABLE 2. *A comparison of average body lengths of mutant rats with their gray Norway controls*

Strain	Sex	N	Mean Length In mm	Standard Error of Mean	Standard Deviation About mean	Difference Between Means	Standard Error of Difference Between Means	Values of t	Probability that the Difference Between Means is Significant
Gray	Male	307	245.53	0.302	5.28	.....	.....	.....	.....
Gray	Female	304	228.36	0.314	5.46	.....	.....	.....	.....
Cinnamon	Male	65	248.96	0.441	3.53	3.43	5.0319	4.9924	Less than .001
Cinnamon	Female	76	231.11	0.343	2.97	3.75	5.0743	4.2258	Less than .001
Curly	Male	76	248.31	0.433	3.57	2.78	5.0003	4.0808	Less than .001
Curly*	Female	84	228.79	0.453	4.13	0.43	5.2144	0.6821	Less than .400
Hooded	Male	17	238.05	1.432	5.72	7.48	5.3024	5.6618	Less than .001
Hooded	Female	19	222.21	0.382	1.67	6.15	5.3289	4.8803	Less than .001
Curly R.E.D.	Male	37	244.21	0.858	5.15	1.11	5.2815	3.3094	Less than .001
Curly R.E.D.	Female	34	224.24	0.212	1.22	4.12	5.2080	4.1843	Less than .001
Curly Hooded*	Male	14	246.20	1.689	6.09	0.67	5.3345	0.4596	Less than .600
Curly Hooded*	Female	8	230.37	2.181	5.77	2.01	5.4858	1.0230	Greater than .300
Alb. Waltzer	Male	16	237.74	1.276	4.94	7.73	5.2819	5.7513	Less than .001
Alb. Waltzer	Female	17	220.25	0.838	3.35	8.11	5.3858	6.0419	Less than .001
Albino	Male	139	239.30	0.539	6.33	6.23	5.6409	10.8274	Less than .001
Albino	Female	124	223.37	0.367	4.07	4.99	5.1083	9.1674	Less than .001

*The significance of the differences between the means in these cases is uncertain.

Because the size drift downward noted in successive generations of mutant albinos applies to length as well as weight, we must examine early generations to learn whether originally albinos were inferior to grays in length. If we examine 80 albino males of the F_0 and F_1 generations of the albino strain, we find that its mean length of 243.60 mm. is inferior to their controls by 1.93 mm. The corresponding 75 albino females of the F_0 and F_1 generations had a mean length of 226.47 mm. which is 1.89 mm. shorter than their control. The 37 curly R.E.D. males had a mean length of 244.21 $\pm$ 0.86 mm., which is inferior to standard by 1.11 mm. The 34 curly R.E.D. females had a mean length of 224.24 $\pm$ 0.21 mm., which is inferior to their control by 4.12 mm. The 14 curly-hooded males had a mean length of 246.20 $\pm$ 1.69 mm., and increase above that of their controls of 0.67 mm. Here the difference is not significant. The 8 curly-hooded females had a mean length of 230.37 $\pm$ 2.18 mm., an increase of 2.01 mm. This difference is not significant. The 16 albino-waltzer males had a mean length of 237.74 $\pm$ 1.28 mm., a decrease from that of their controls of 7.73 mm. The 17 albino-waltzer females have a mean length of 220.25 $\pm$ 0.84 mm., a decrease from the mean of their controls of 8.11 mm.

If we look for the negating effects of the R.E.D. gene upon the increaser effects of the curly gene, we see in Chart 4 that starting with a gray male control length of 245.52 mm., curly raises this to 248.31 mm., and R.E.D. added to curly reduces it again to 244.21 mm., which is below the mean of the gray Norway control. If we examine the same phenomena in females, we see that starting with a mean body length in gray Norways of 228.36 mm., curly increases this slightly to 228.79 mm. (which is not statistically significant), and that the addition of the R.E.D. gene to curly reduces mean length to 224.24 mm., which is far below the mean of the controls. If we look for similar reducing effects of the hooded gene (Chart 5) in negating the increase produced by the curly gene, we find that starting with a mean body length of 245.53 mm. in gray Norway males, the curly gene raises mean body length to 248.31 mm., but the addition of the hooded gene to the curly gene reduces it to 246.20 mm., which is almost down to the mean of the gray Norway controls. In this case the reducing effect of the hooded gene is less than that of the R.E.D. gene when combined with curly. Correspondingly for females, starting with a female gray Norway mean length of 228.36 mm., the curly gene raises this to 228.79 mm. (which is not significant), but the addition of the hooded gene is unable to reduce it, the curly-hooded mean being 230.37 mm. If we examine the reducing effects of waltzer when added to albino in Chart 6, we see that starting with a gray Norway mean length of 245.53 mm. (employing F_0 and F_1 albino data) the albino gene reduces it to 243.60 mm., and the addition of the waltzer gene further reduces it to 237.74 mm. Correspondingly, starting with a female control mean length of 228.36 mm., the substitution of the albino gene for its pigment-

TABLE 3. *A comparison of average lengths of mutant strains with each other necessary for preparing Charts 1-6*

Strains Compared				Standard Error of Difference Between Means	Values of t	Probability That the Difference Between Means is Significant
Curly	Male	vs	Curly R.E.D. Male	4.5716	4.2512	Less than .001
Curly	Female	vs	Curly R.E.D. Female	3.6072	6.2587	Less than .001
Curly	Male	vs	Curly Hooded Male	3.6397	1.9932	.050
Curly	Female	vs	Curly Hooded Female*	4.3450	0.9827	Less than .300
Albino	Male	vs	Alb. Waltzer Male*	6.2413	0.9467	.300
Albino	Female	vs	Alb. Waltzer Female	4.0185	3.0021	Less than .001
Alb(F_o+F_1)	Male	vs	Alb. Waltzer Male	3.4134	6.2688	Less than .001
Alb(F_o+F_1)	Female	vs	Alb. Waltzer Female	1.6717	13.8512	Less than .001
Alb(F_o+F_1)	Male	vs	Gray Male	4.8882	7.0938	Less than .001
Alb(F_o+F^1)	Female	vs	Gray Female	4.9194	2.9799	Less than .010

*The significance of the differences between the means in these cases is uncertain.

TABLE 4. *A comparison of average weights of mutant strains with each other necessary for preparing Charts 1-6*

Strains Compared				Standard Error of Difference Between Means	Values of t	Probability That the Difference Between Means is Significant
Curly	Male	vs Curly R.E.D.	Male	31.8414	3.8806	Less than .001
Curly	Female	vs Curly R.E.D.	Female	18.7501	4.6181	Less than .001
Curly	Male	vs Curly Hooded	Male	33.2212	1.0282	Greater than .050
Curly	Female	vs Curly Hooded	Female	23.1641	2.5773	.010
Albino	Male	vs Alb. Waltzer	Male	29.7930	2.4377	Greater than .010
Albino	Female	vs Alb. Waltzer	Female	14.0842	2.3637	Greater than .020
Alb(F_+ F_1)	Male	vs Alb. Waltzer	Male*	17.2690	0.1057	.900
Alb(F F_1)	Female	vs Alb. Waltzer	Female*	11.5236	0.0484	.900
Alb(F_0+F_1)	Male	vs Gray	Male	28.3880	5.0064	Less than .001
Alb(F_0+F_1)	Female	vs Gray	Female	22.7934	19.0856	Less than .001

*The significance of the differences between the means in these cases is uncertain.

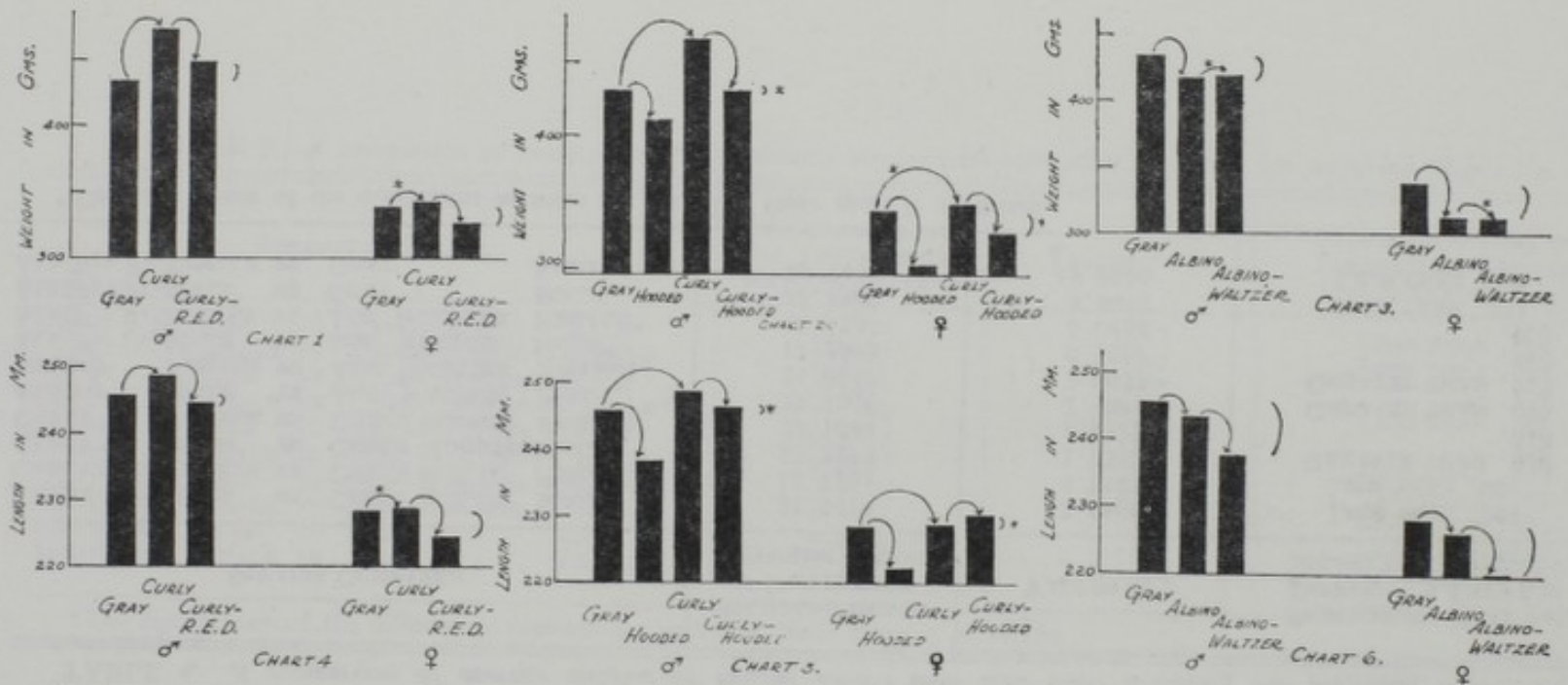


Chart 1. The increaser-effect of the curly gene is significantly reduced in males and more than completely negated in females by the addition of the R.E.D. gene in curly-R.E.D. rats. Chart 2. The increaser-effect of the curly gene is canceled by the decreaser-effect of the hooded gene in both male and female curly-hooded rats. Chart 3. The decreaser-effect of the albino gene is not modified by the addition of the waltzer gene in both male and female albino-waltzer rats. Chart 4. The increaser-effect of the curly gene is more than negated in both males and females by the addition of the R.E.D. gene in curly-R.E.D. rats. Chart 5. The increaser-effect of the curly gene is negated by the decreaser-effect of the hooded gene in curly-hooded male rats. The slight increaser-effect of the curly gene is not reduced by any decreaser-effect of the hooded gene in curly-hooded female rats. In fact, curly-hooded females are found to be longer than curly females, but the difference is not statistically significant. Chart 6. The decreaser-effect of the albino gene is greatly accentuated by the addition of the waltzer gene in albino-waltzer rats.

producing allel reduces it to 226.47 mm. and the addition of the waltzer gene reduces mean length still further to 220.25 mm.

These effects of coat-character genes on body length may be listed as follows:

A. Length increasing effects associated with:
   1. Cinnamon in male and female
   2. Curly in male (possibly in female)

B. Length decreasing effects associated with:
   1. Hooded in male and female
   2. Albino in male and female
   3. Ruby-eyed dilute in male and female (known by its effect on curly)
   4. Waltzer in male and female (known by its effect on albino

Summary

It has been shown in this paper that when the data on mutant strains, summarized in chart form by Keeler and King in 1941, are compared with a gray Norway control, the presence of single genes for curly and cinnamon produce statistically significant increases in body weight. The presence of genes for hooded, ruby-eyed dilute, and albino have a reducing effect on body weight. Waltzer is neutral in that it has practically no effect on weight.

It has been shown further that in the cases of cinnamon and curly the increase in weight is accompanied by a corresponding increase in body length. In the cases of hooded, ruby-eyed dilute, and albino the reduction in weight is accompanied by a corresponding decrease in body length. Waltzer is a reducer gene for length.

All the effects on weight and length are unaffected by sex.

In strains bearing simultaneously several of the coat-character genes named above the results of plus and minus effects on weight are as follows:

1. Ruby-eyed dilute cancels the weight increase produced by curly in both sexes.
2. Hooded cancels the weight increase produced by curly in both sexes.
3. Waltzer leaves unaltered the weight decrease produced by albino in both sexes.

In strains bearing simultaneously several of the coat-character genes named above, the results of plus and minus interactions on body length are as follows:

1. Ruby-eyed dilute cancels the length increase produced by curly in both sexes.
2. Hooded cancels the length increase produced by curly in both sexes.
3. Waltzer exaggerates the length decrease produced by albino in both sexes.

Acknowledgement

For the standard errors of the difference between the means, together with their probabilities, appearing in this paper, I am indebted to the kindness of Professor H. M. Lufkin of the University of Pennsylvania.

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X

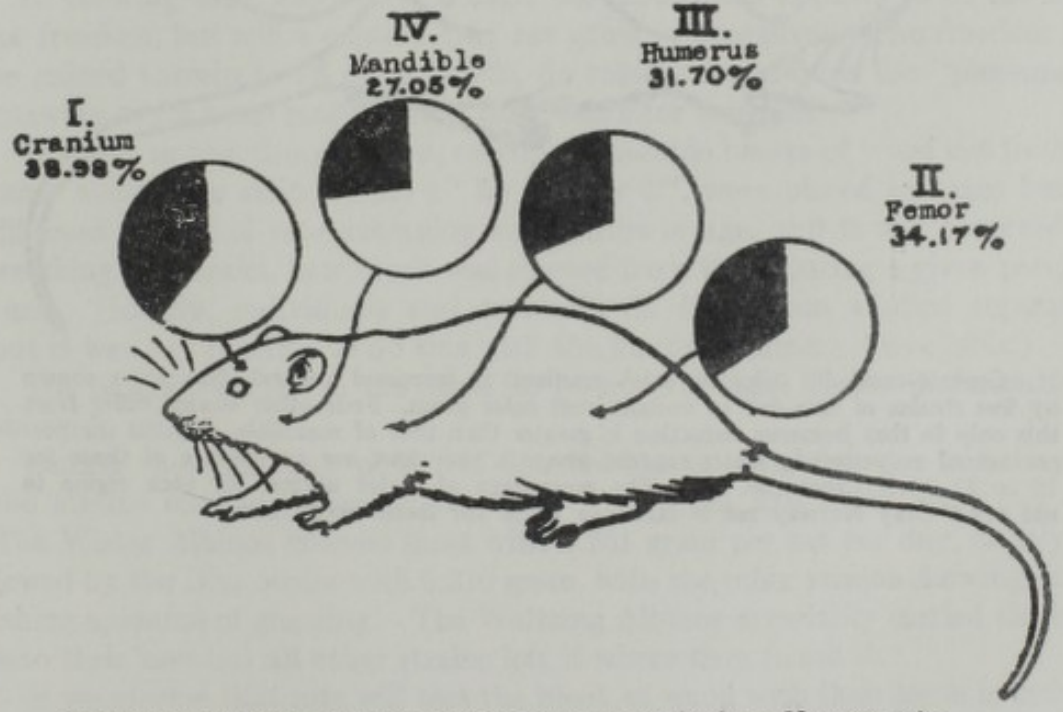
OSSEO-DESICCATION AND SOCIOMETRY

In a paper published in the February issue of SOCIOMETRY, I mentioned the possibility of natural desiccation affecting interpersonal behavior, but I did not describe the exact nature of such desiccation which is modified by coat color genes. In reply to this article inquiry has been made for details.

The nature of these facts can be best illustrated by two diagrams that I prepared in 1941 for an unpublished paper entitled "The effects of certain coat color genes on the normal rate of water loss in the skeleton of the Norway rat." Diagram "A" represents graphically by means of black sectors the standard percentage of water found respectively in the cranium, mandible, humerus and femor of adult, gray Norway rats. The descending order of water percentage is cranium, femor, humerus, mandible.

Diagram "B" represents graphically by means of black sectors the decrease in average percentage of water found respectively in cranium, mandible, humerus and femor of twenty to twenty-two adult Cinnamon rats, in the case of each bone taking percentage of water normal for the comparable adult, gray rat standard as one hundred percent.

It will be noted in diagram "B" that the increase in natural osseo-desiccation accompanying the presence of the Cinnamon gene follows a

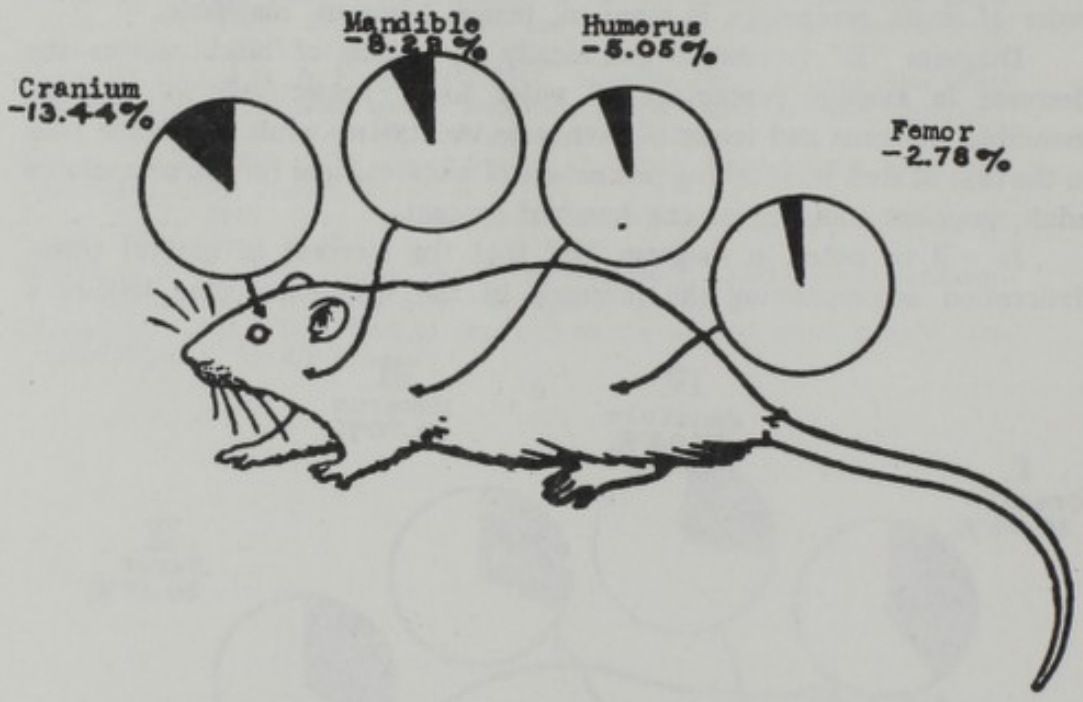


Relative percentages of water in the bones of adult Gray Norway rats.

cephalo-caudadly oriented, axial gradient, that is, the Cinnamon gene has a decreasing degree of effect upon the normal water percentage in cranium, mandible, humerus and femor.

Five strains of rats containing coat color mutations were found to have an effect identical with that of the Cinnamon gene. Four other strains of rats containing coat color mutations were found to differ from the condition described in diagram "B" only in that reduction of water percentage for humerus is greater than that for mandible.

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Cephalo-caudadly oriented axial gradient of increased natural desiccation shown by five strains of rats due to mutant coat color genes. Four other strains differ from this only in that humerus reduction is greater than that of mandible. Figures for percentage of reduction in water content given in the chart are an average of those for 20 to 22 adult Cinnamon rats. The percentage of water normal for each region in the adult Gray Norway rat is taken as 100% for these comparisons.

XI

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NOTE ON GNAWING IN THE GRAY NORWAY RAT AND ITS COAT-CHARACTER DERIVATIVE STRAINS

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Gnawing is so characteristic of rats and their relatives such as the mice, rabbits, squirrels, jerboas, beavers and porcupines, that the whole order of rodents derives its name from this unique propensity. Indeed, the ever-growing type of incisors that these rodents bear, virtually destines them to gnaw sufficiently or die. This conclusion is reached because of the fact that in individual rats, rabbits, and guinea pigs in which the upper and lower incisors do not appose properly, the incisors continue to grow, often piercing the skull or locking the jaw, and in most cases interfering with the normal intake of food.

It is known that if several wild gray Norway rats are placed in white pine cages ½ inch thick, they may gnaw their way out during a single night. This is true also of Mutant Albinos derived from the gray Norway strain by mutation in a single genetic locus. As a result of this highly developed tendency to gnaw, gray Norways and Mutant Albinos are ordinarily housed in armored cages. Curiously enough, in contrast to the Mutant Albinos, all other coat-character mutant strains derived from the gray Norway present no more of a housing problem than do ordinary strains of tame laboratory rats.

In chewing their way out of a cage, the motivation appears to be the desire for freedom, but will a captive gray rat gnaw so excessively if no freedom is to be gained thereby? In other words, do rats ever gnaw for the "pleasure" of gnawing or for some motive other than desire for freedom?

In order to test this question, small, comparable blocks of wood cut from the same white pine strip, about 1″ by 2¼″ by 5″, were placed in cages bearing different strains of rats averaging six months of age, and it was observed, by weighing the blocks, how much was chewed from them during a given period of time. (Ideally, individuals and sexes should have been studied separately, but it was not possible to do this with the limited equipment available.)

The blocks were left in the cages for a period of eight days. The results are shown in table 1.

During the eight day period of observation the gnawing per individual of the strains studied, averaged between 0.023 gram and 0.261 gram per day. The Wistar Albinos gnawed most with 0.261 gram per rat per day, closely followed by the Blue strain with 0.210 gram, with the other strains showing diminishing amounts of gnawing. The Waltzing Albinos invariably carried the block into their nest but all other strains left it where they found it.

If we assume that rats will test the block of wood with their teeth in order to see if it is good for food, then we might expect to find a great amount of gnawing on the first night and thereafter very little gnawing. From the table it is found

to be true that all breeds gnawed more the first night than on subsequent nights. On the first night Wistar Albinos gnawed more than ten times as much as gray rats, and no strain gnawed nearly as little as gray rats. This behavior of gray—compared with Wistar Albino—is just the reverse of the gnawing activity observed when freedom is the goal to be obtained, in which case gray rats gnawed enormously, and other strains, save Mutant Albino, gnawed very little. The Mutant Albino on the first night, curiously enough, gnawed the block eight times as much as the gray. The Red Eyed Yellow gnawed eight times as much on the first night as the grays and thereafter even less than the grays.

TABLE 1

NUMBERS OF RATS		STRAIN	AMOUNT REMOVED FROM BLOCK IN GRAMS/RAT/DAY FOR 8 DAYS	AMOUNT GNAWED THE FIRST 24 HOURS IN GRAMS/RAT	AMOUNT REMOVED FROM BLOCK AFTER FIRST 24 HOURS IN GRAMS/RAT/DAY	AMOUNTS OF GNAWING AFTER FIRST 24 HOURS IN TERMS OF GRAY GNAWING TAKEN AS 1
Males	Females					
8	7	Curly	0.116	0.266	0.095	5
2	5	Mutant Albino	0.098	0.500	0.051	3−
1	7	Red Eyed Yellow	0.078	0.563	0.0089	½
6	5	Blue	0.210	0.273	0.201	11
6	10	Albino Waltzer	0.129	0.285	0.098	5
2	8	Cinnamon	0.044	0.200	0.0214	1+
19	13	Gray	0.023	0.062	0.0178	1
7	7	Wistar	0.261	0.642	0.206	11
10	7	Hatai (black piebald)	0.075	0.235	0.0525	3−

After the first 24 hours in which, presumably, their curiosity was satisfied and during which time they found that chewing the block had nothing to do with freedom, the Red Eyed Yellow rats chewed during seven days one half as much as the grays, whereas Curly chewed 5, Mutant Albino 3−, Blue 11, Albino Waltzer 5, Cinnamon 1+, Wistar Albino 11, and Hatai 3− times as much as the grays.

CONCLUSION

It is concluded that chewing for "pleasure" or other non-utilitarian motives is a strongly developed characteristic in Wistar Albinos and Blues, developed less strongly in the other coat-character mutant strains studied and almost undeveloped in gray Norways.

XII

SÉANCE DU 28 JANVIER 1947

LES MODIFICATIONS DE LA LONGUEUR DE LA QUEUE EN COMPARAISON DE LA LONGUEUR DU CORPS CHEZ LE RAT NORVEGIEN

PAR

Clyde E. KEELER

INTRODUCTION

Un des traits caractéristiques que DARWIN a cru imprimé sur certaines espèces d'animaux domestiques comme le résultat de compression Lamarckienne du milieu protecteur et artificiel de la captivité, a été l'amoindrissement de la longueur de la queue relative à la longueur du corps. On a remarqué ce phénomène dans les queues qui portent des ganglions, chez le rat de l'Isle de Man, le chat siamois, le chat japonais, le bulldog anglais, et aussi dans la queue qui ne porte pas de ganglions, chez le porc domestique.

Quand le Dr Henry H. DONALDSON (qui a visité et parlé avec Darwin) a commencé ses investigations de phénomènes Lamarckiens chez le rat blanc de laboratoire, il s'est étonné de remarquer que la queue du rat domestique est plus longue dans les deux sexes que chez le rat gris sauvage norvégien, dont les races albinos de nos laboratoires scientifiques sont dérivées. Ainsi, la proportion queue-corps dans la race albinos Wistar est exactement le contraire de ces modifications observées par DARWIN chez d'autres animaux, modifications où il a vu la marque indélébile de la domestication.

Parce qu'on ne voit pas de règle universelle dans cette relation queue-corps modifiée, nous avons examiné les chiffres retenus sur ce sujet, mais non étudiés, par DONALDSON. Nous avons publié autrefois des comparaisons queue-corps en général, mais pas les détails.

Dans ces comparaisons, nous avons employé la méthode contrôle par paire ; c'est-à-dire, comme contrôle de chaque individu dans une population mutante, nous avons sélectionné un individu gris norvégien de la même longueur de corps et d'un âge aussi comparable que possible. Ces animaux contrôlés sélectionnés de cette manière, ont composé la population de contrôle. Les chiffres calculés pour comparaison sont donnés dans le tableau 1.

Nos résultats mènent à la conclusion que les déterminants génétiques qui modifient les couleurs du poil, s'ils font la queue plus longue ou plus courte, peuvent rompre définitivement le mécanisme normal qui coordonne les processus de la croissance de la queue et du corps.

BULL. SOC. ZOOL. FRANCE. LXXII. 1947. pp. 31-35.

Soixante et un mâles canelles (cinnamon) qui possèdent une longueur moyenne de la queue de 193,11 ± 1,1 mm., excèdent 61 contrôles gris d'une longueur moyenne de la queue de 192,23 ± 1,2. La différence est 0,88 mm., seulement 0,5 fois plus grande que l'erreur permise (standard) de 1,6 mm.

Soixante-quatorze femelles canelles avec une longueur moyenne de la queue de 187,36 ± 0,9 mm. excèdent 74 contrôles gris d'une longueur moyenne de la queue de 186,64 ± 0,9 mm. La différence est 0,72 mm., seulement 0,50 fois plus large que l'erreur permise de 1,3 mm.

Les 135 canelles (mâles et femelles) ont une longueur de la queue de 189,96 mm. et leurs 135 contrôles gris possèdent une longueur moyenne de la queue de 189,22 mm. La différence est seulement 0,74 mm.

Quarante-six mâles bouclés (curly) d'une longueur moyenne de la queue de 189,30 ± 1,1 mm., excèdent la longueur moyenne de la queue chez les 46 contrôles de 190,70 ± 1,5 mm. La différence de 1,40 mm. est seulement 0,8 fois plus grande que l'erreur permise de 1,8 mm.

Cinquante et une femelles bouclées d'une longueur de la queue de 180,30 mm. excèdent par 1,13 mm. 51 contrôles gris qui possèdent une longueur moyenne de la queue de 179,20 mm.

Cinquante-huit mâles (bouclé-bonnet) d'une longueur de la queue de 184,20 ± 1,1 mm. sont plus courts que 58 contrôles gris qui possèdent une longueur moyenne de la queue de 185,87 ± 1,4 mm. La différence de 1,67 mm. est seulement 0,9 fois plus grande que l'erreur permise de 1,8 mm.

Cinquante-quatre bouclé-bonnet femelles d'une longueur de la queue de 182,60 mm., sont plus courts que 54 contrôles gris qui possèdent une longueur moyenne de la queue de 181,80. La différence est seulement 0,80 mm.

Vingt-huit mâles bonnet (hooded) d'une longueur de la queue de 186,39 ± 1,2 mm., sont plus petits que 28 contrôles gris de 189,92 ± 1,3 mm. La différence est 3,53 mm. Celle-ci est 2,1 fois plus grande que l'erreur permise de 1,6 mm. Cette différence a de la signification statistique.

Quatre-vingt-six bonnets et bouclé-bonnet mâles d'une longueur de la queue de 184,89 ± 0,7 mm., sont plus courts que 86 contrôles gris qui possèdent une longueur moyenne de la queue de 187,32 mm. La différence de 2,43 mm. est 2,7 fois plus grande que la différence permise de 1,4 mm.

Cent quatre mâles (dont 58 possèdent aussi le poil bonnet) d'une longueur moyenne de 186,47 ± 0,8 mm. sont inférieurs à 104 contrôles gris avec une longueur moyenne de la queue de 188,05

± 1,0 mm. La différence est 1,58 mm. ou 1,3 fois plus grande que l'erreur permise de 1,2 mm.

Entre les 9 populations décrites ci-dessus, deux groupes seulement montrent une différence en longueur de la queue plus grande que celle du rat gris norvégien. Ces deux populations sont mâle bonnet et mâle bonnet (58 de la race bouclé-bonnet inclus) et les deux populations mutatées ont la queue plus courte que celle des populations contrôles grises.

Trente-cinq mâles albinos Wistar d'une longueur moyenne de la queue de 193,52 ± 1,1 mm., excèdent 35 gris avec une longueur de la queue de 181,31 ± 1,6 mm. La différence 12,21 mm. ou 6,4 fois plus grande que l'erreur permise de 1,9 mm.

Trente et une femelles albinos Wistar, d'une longueur de la queue de 184,52 ± 3,2 mm., excèdent 31 contrôles gris avec une longueur moyenne de la queue de 166,51 ± 1,4 mm. La différence est 18,01 mm., ou 5,1 fois plus grande que l'erreur permise de 3,2.

Cent quatre-vingt-trois vieux mâles albinos Wistar d'une longueur moyenne de la queue de 211,29 ± 1,8 mm., excèdent 183 gris contrôles avec 188,86 ± 0,3 mm. La différence est 22,43 mm. ou 12,5 fois plus grande que l'erreur permise de 1,8 mm.

Deux cent trente et une vieilles femelles albinos Wistar, d'une longueur de la queue de 193,14 ± 0,8 mm., excèdent 231 contrôles gris avec une queue de 178,03 ± 0,3 mm. de long. La différence est 15,11 mm., ou 18,8 fois plus longue que l'erreur permise de 0,8 mm.

Avec cette méthode contrôle par paire employée ci-dessus, on peut confirmer l'observation de Donaldson que la queue de la race albinos Wistar est plus grande que la queue du rat gris norvégien. On trouve cette condition dans quatre populations (deux populations mâles et deux populations femelles).

Il est évident aussi que la longueur moyenne de la queue du mâle de la race albinos Wistar adulte accroît de 12,2 ± 1,9 mm. jusqu'à 22,43 ± 1,8 mm. dans les vieux mâles. Cette augmentation a de la signification parce que la différence de 10,22 mm. est 3,9 fois plus grande que l'erreur permise de 2,6 mm. Néanmoins, la relation queue-corps a diminué un petit peu (de 78,80 0/0 jusqu'à 77,33 0/0) ; ce qui indique une altération des relations hétérogoniques de l'accroissement de la queue et du corps.

Il semble que la différence actuelle entre les femelles albinos Wistar et leurs contrôles gris norvégiens amoindrisse de 18,01 ± 3,2 mm. jusqu'à 15,11 ± 0,8 mm. Cette diminution n'a pas de signification parce que la différence de 2,9 mm. est seulement de 0,9 fois plus grande que l'erreur permise de 3,3 mm. Néanmoins, la relation queue-corps a augmenté un petit peu (de 80,06 0/0 jusqu'à

81,32 0/0). Ce fait semble indiquer une altération des relations hétérogoniques de l'accroissement de la queue et du corps.

Race	Nombre d'individus	Longueur moy. du corps	Longueur moyenne de la queue de mutantes	Longueur moyenne de la queue de contrôles	Différence entre la longueur de la queue de mutantes et de contrôles	Différence divisée par l'erreur permise
Canelle ♂ . . .	61	249,13	193,11 ± 1,1	192,23 ± 1,2	0,88 ± 1,6	0,5
Canelle ♀ . . .	74	231,02	187,36 ± 0,9	186,64 ± 0,9	0,72 ± 1,3	0,5
Tous les animaux Canelles . . .	135	239,20	189,96	189,22	0,74	
Bouclé ♂ . . .	46	245,34	189,30 ± 1,1	190,70 ± 1,5	1,40 ± 1,8	0,8
Bouclé ♀. . . .	51	217,72	180,30	179,20	1,13	
Bouclé-Bonnet ♂ .	58	240,20	184,20 ± 1,1	185,87 ± 1,4	1,67 ± 1,8	0,9
Bouclé-Bonnet ♀ .	54	225,68	182,60	181,80	0,80	
Bonnet ♂ . . .	28	243,46	186,39 ± 1,2	189,92 ± 1,3	3,53 ± 1,6	2,1
Bonnet et Bouclé-Bonnet ♂ . .	86	241,26	184,89 ± 0,7	187,32 ± 0,5	2,43 ± 1,4	2,7
Bouclé et Bouclé-Bonnet ♂. . .	104	242,48	186,47 ± 0,8	188,05 ± 1,0	1,58 ± 1,2	1,3
Albinos Wistar ♂ .	35	230,08	193,52 ± 1,1	181,31 ± 1,6	12,21 ± 1,9	6,4
Albinos Wistar ♀ .	31	206,97	184,52 ± 3,2	166,51 ± 1,4	18,01 ± 3,2	5,1
Vieux Albinos Wistar ♂	183	244,21	211,29 ± 1,8	188,86 ± 0,3	22,43 ± 1,8	12,5
Vieux Albinos Wistar ♀	231	218,91	193,14 ± 0,8	178,03 ± 0,3	15,11 ± 0,8	18,8

Résumé

Une comparaison des relations entre la longueur de la queue et la longueur du corps dans plusieurs races mutantes du rat norvégien a amené les conclusions suivantes :

1) Le rat mâle bonnet porte la queue relativement plus courte que celle du rat mâle gris norvégien, dont la race bonnet est récemment dérivée.

2) Le rat albinos Wistar (mâle et femelle) porte la queue relativement plus longue que celle des rats gris norvégiens, de quelle race les albinos sont anciennement dérivés.

3) L'accroissement de la longueur de la queue observé dans les mâles et femelles adultes et vieillards est devenu plus excessif avec l'âge, mais la relation queue-corps dans les vieux rats est un peu plus petite que dans les albinos adultes. L'accroissement des différences entre la longueur de la queue des albinos adultes et des vieux albinos a de la signification.

4) Les albinos portent trois paires de déterminants mendéliens qui se manifestent dans la couleur du poil.

Parce que la queue de la race albinos Wistar s'accroît en longueur

relative à la longueur de corps, et parce que le déterminant noir probablement diminue la queue dans tous les deux sexes, il est naturel de supposer que la cause de l'accroissement de la queue albinos Wistar se trouve dans les déterminants génétiques de même sorte aussi. C'est dire que les autres déterminants mendéliens qui ne se manifestent pas dans le poil, se manifestent dans la proportion queue-corps et dominent sur les tendances diverses des déterminants bonnet et noirs.

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XIII

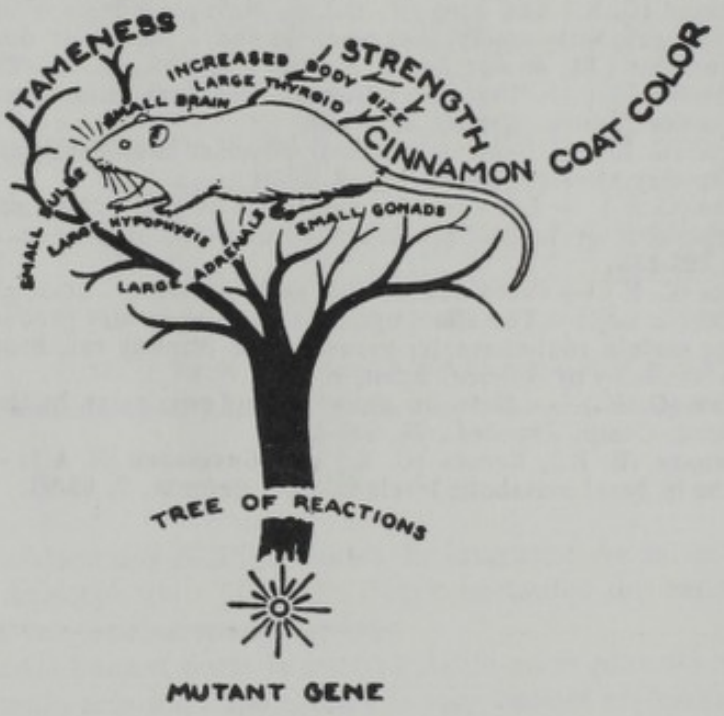
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MODIFICATION OF BRAIN AND ENDOCRINE GLANDS, AS AN EXPLANATION OF ALTERED BEHAVIOR TRENDS, IN COAT-CHARACTER MUTANT STRAINS OF THE NORWAY RAT[1]

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INTRODUCTION

In a number of contributions (Keeler and King, 1941-1942; Keeler, 1942; Keeler, 1945; Shopback, Keeler, and Greenberg, 1943;

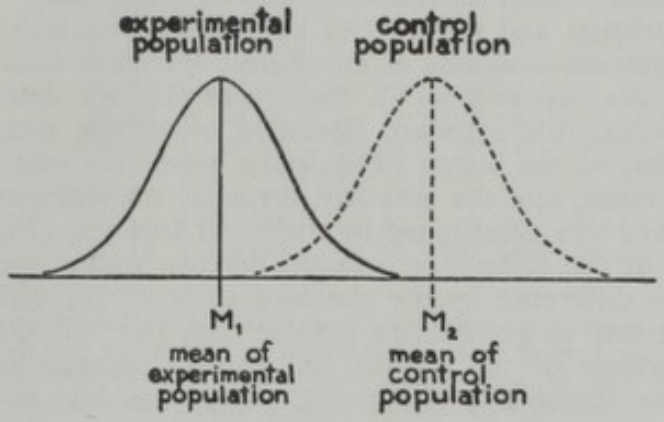


Keeler, 1947), the author and his associates have shown that certain coat-character genes manifest themselves in all parts of the mammalian organism by producing modifications of morphology. They have demonstrated that these coat-character mutants may have modified physiological natures, as well as certain modified trends in behavior. We may represent diagrammatically the effects of a single gene upon development and on consecutive chains of reaction, by means of the branching of a tree as is shown here for the cinnamon gene (Fig. 1). The tips of the twigs represent behavior charac-

[1]This paper was awarded the competitive research prize of the Association of Southeastern Biologists, before which organization it was read April 19, 1947.

teristics such as tameness and the fully developed organs with which the Norway rat carries on the business of life. According to this view, the mutated or altered gene initiates a complex series of altered bio-chemical reactions, these reactions setting off still other altered reactions and so on.

The mechanism of total development in terms of genes is much more complicated than this because we know that all physical characteristics are affected by numerous genes, each giving rise to complex trees of reaction. Many of these genes (possibly most of them) interact with each other. An altered hereditary factor or gene produces its altered developmental reactions throughout the whole body of the animal, altering such things as body size, relative proportions of bodily parts, glands, sense organs, brain, and hair color. Some of



$$E_{diff} = \sqrt{E_1^2 + E_2^2}$$

E_{diff} = standard error of difference between two populations
E_1 = " " " mean of experimental population
E_2 = " " " " " control population

$$\text{significance} = \frac{M_2 - M_1}{E_{diff}} => 2$$

these structural changes, in turn, modify physiology and the modified physiology produces altered behavior trends, some of which are measurable. If one removes the mutant hair color genetically, one automatically lifts out the whole tree of associated reactions and effects, including the mutant gene that caused them.

Not only may the experimenter, by means of the coat-color handle, lift out several trees of altered gene reactions, but he may also combine them together by means of genetic techniques in order to synthesize new, combinational trends in morphology and behavior. Because the physical bases for such altered behavior trends are simply inherited, and may be compounded by the combining together of different mutant coat-character genes in individuals and strains, we

may direct the evolution of the behavior of this mammalian species, and conceivably even that of man.

Materials and Methods

In this paper we plan to examine statistically certain autopsy measurements upon members of nine mutant strains of Norway rats, all descended from coat-character mutants appearing in an inbred stock of gray animals originally caught in the wild. Data on four other strains are too meagre for statistical treatment. These rats have been described previously by the author and his associates in the scientific contributions referred to above. For making comparisons we have employed the paired-control method. This consists of choosing from a large group of gray Norway rats of the source strain, one individual of similar age and identical body length for each animal in the coat-character mutant group under study. The mutant population and the control population so selected are compared with respect to details of structure. For each measurement in mutant animals, as well as in their controls, we determined the arithmetic mean, the standard deviation about the mean, and the standard error of the mean. The lesser mean was subtracted from the greater mean, and the standard error of the difference between the two means was determined by the usual formula (Fig. 2). The significance of the difference between the two means was found by dividing this difference by the standard error of the difference. If the quotient was as great as or greater than two, the difference between the means of the mutant and control populations was considered to be statistically significant. If it was less than two, the difference was regarded as insignificant.

Results

The mean values for various mutant measurements have been determined and compared with the mean values for control measurements in such a way as to discover their percentage relation to the mean control measurements. The results have been given in a series of tables (Tables 1-4). When a number is in italics in the tables, its deviation from the gray Norway rat is statistically significant. When a number is in black face type, its deviation from the gray Norway value is not significant. When the number is in regular type, the mean value is based on too few animals to permit statistical examination. It will be noted that these measurements include: weights of brain, olfactory bulbs, paraflocculus, residual brain weight (when alterations in bulbs, paraflocculus, and water content are accounted for), percentage of water in the brain, and weights of hypophysis, thyroids, adrenals, and gonads. Of the 144 populations of measurements of mutants and their corresponding gray controls compared in the statistically treated data, 112 differences or 78 percent are significant. Thirty-two or 22 percent are not significant and only five of these latter deviations are as great as 2 percent of the gray value.

If we examine the tendencies shown in Table 5, we find: *brain,* more often reduced than enlarged; *olfactory bulbs,* almost invariably reduced in males, but more often enlarged in females; *paraflocculi,* almost invariably enlarged in both sexes; *residual brain weight,* more often reduced; *hypophysis,* almost invariably enlarged; *thyroids,* more often reduced than enlarged; *adrenals,* almost equally divided in males but more frequently reduced in females; *gonads,* almost

TABLE 1. *Mean values for statistical populations of weights of various organs and also of percentage of water in the brain from males of mutant strains of Norway rats, converted into percentages of the corresponding mean gray control value which is taken in each case as one hundred percent*

Strain	Cinnamon	Curly	Hooded	Fawn	Black	R. Eye Dil.
No. of rats	60	78	17	15	3	3
Brain	99.20	97.58	93.03	**100.16**	93.53	95.79
Olf. bulbs	96.14	94.75	79.44	**100.00**	96.60	101.92
Parafloc	103.71	101.45	107.72	105.65	105.88	95.18
Resid. brain	**99.83**	98.20	96.31	**100.64**	94.34	95.45
% water brain	**100.00**	99.36	**99.90**	99.74	100.28	99.75
Hypophysis	103.85	116.35	**102.02**	110.97	76.83	93.18
Thyroids	105.73	108.01	73.41	67.06	70.13	66.25
Adrenals	108.11	106.26	83.66	97.65	91.12	88.10
Gonads	87.52	101.48	91.16	**101.54**	98.34	90.38

TABLE 2. *Mean values for statistical populations of weights of various organs and also of percentage of water in the brain from females of mutant strains of Norway rats, converted into percentages of the corresponding mean gray control value which is taken in each case as one hundred percent*

Strain	Cinnamon	Curly	Hooded	Fawn	Black	R. Eye Dil.
No. of rats	69	84	19	11	3	2, 3
Brain	99.07	97.69	94.41	**99.79**	98.31	94.75
Olf. bulbs	103.50	103.41	92.86	104.36	112.49	110.14
Parafloc	103.00	103.46	113.07	107.19	114.96	94.60
Resid. brain	**99.64**	98.08	**100.59**	**99.99**	97.59	94.75
% water brain	**100.00**	99.18	99.19	99.74	100.06	99.56
Hypophysis	116.19	111.76	104.21	105.62	108.54	87.10
Thyroids	**98.79**	109.48	122.77	74.50	54.31	51.90
Adrenals	**104.68**	97.85	86.73	91.50	99.22	106.22
Gonads	**102.74**	107.46	92.39	113.03	99.27	65.75

evenly divided in males but most often enlarged in females. When one examines the changes in particular strains one finds that the modifications are unique for each strain, but definitely hyperglandular strains may be recognized such as cinnamon, curly, and waltzer. Hypoglandular strains include hooded, black, R.E.D., and mutant albino.

Discussion

The well-known vicious nature of curly rats is correlated with their hyperglandular condition, whereas the docile nature of blacks

TABLE 3. *Mean values for statistical populations of weights of various organs and also of percentage of water in the brain from males of mutant strains of Norway rats, converted into percentages of the corresponding mean gray control value which is taken in each case as one hundred percent*

Strain	Hairless	Mut. Alb.	Bl. Hooded	Curly R.E.D.	Curly Hooded	Alb. Waltzer	Wistar Albino
No. of rats	3	146	15–42	37	14	12, 16	10
Brain	104.47	101.05	88.32	101.72	96.96	**98.49**	96.38
Olf. bulbs	104.37	92.69	96.58	90.18	81.92	94.49	67.44
Parafloc	113.76	**100.40**	94.75	101.42	**100.59**	**100.00**	80.54
Resid. brain	103.96	.....	**88.36**	100.94	**97.64**	.....	.....
% water brain	100.41	.....	.....	99.74	99.51	100.39	.....
Hypophysis	122.61	96.26	104.76	117.82	108.82	105.55	107.06
Thyroids	131.49	92.66	**100.00**	133.57	104.25	115.32	120.17
Adrenals	64.75	93.25	59.17	132.12	107.56	**101.32**	52.13
Gonads	84.15	98.41	75.49	105.85	96.50	105.53	82.90

TABLE 4. *Mean values for statistical populations of weights of various organs and also of percentage of water in the brain from females of mutant strains of Norway rats, converted into percentages of the corresponding mean gray control value which is taken in each case as one hundred percent*

Strain	Hairless	Mut. Alb.	Bl. Hooded	Curly R.E.D.	Curly Hooded	Alb. Waltzer	Wistar Albino
No. of rats	2	132	14-47	34	5, 8	13, 15	10
Brain	96.75	**100.25**	88.52	102.97	**97.80**	**100.64**	97.03
Olf. bulbs	98.84	93.03	114.90	92.08	.....	104.17	75.55
Parafloc	111.68	101.75	109.84	**100.00**	112.88	103.93	76.34
Resid. brain	96.58	.....	**55.00**	103.12	96.22	.....	.....
% water brain	100.27	.....	.....	99.37	99.31	**99.83**	.....
Hypophysis	107.32	**101.63**	133.33	115.46	114.57	**100.00**	161.20
Thyroids	91.37	**99.51**	75.13	140.27	108.36	111.28	120.17
Adrenals	59.89	**98.33**	69.26	105.50	94.63	89.93	67.82
Gonads	79.56	102.51	125.49	104.17	91.62	96.22	77.14

TABLE 5. *Numbers of populations of measurements on mutant rats classified according to the deviation of their means from the means of their corresponding gray Norway control populations*

Characters	Significantly larger than Gray	Larger than Gray	Identical with Gray	Smaller than Gray	Significantly smaller than Gray
MALES:					
Brain	2	1	0	1	5
Olfact. bulbs	0	0	1	0	8
Parafloc.	5	2	1	0	1
Resid. Brain Wt.	1	1	0	3	2
% Water in Brain	1	0	1	1	4
Hypophysis	8	1	0	0	0
Thyroids	5	0	1	0	3
Adrenals	4	1	0	0	4
Gonads	3	1	0	0	4
Totals	29	7	4	5	31
FEMALES:					
Brain	1	2	0	2	4
Olfact. Bulbs	5	0	0	0	3
Parafloc.	7	0	1	0	0
Resid. Brain Wt.	1	0	1	3	1
% Water in Brain	0	0	1	0	4
Hypophysis	6	1	1	0	0
Thyroids	4	0	0	2	2
Adrenals	2	0	0	1	5
Gonads	5	1	0	0	2
Totals	31	4	4	8	21

TABLE 6. *Mean values for various measurements in terms of percentage of their corresponding control means for males of hooded, black, and mutant albino strains of rats, to be compared with Wistar albino values (extreme right column)*

Strain	Hooded	Black	Mutant Albino	Wistar Albino
Brain	93.03	93.53	101.05	96.38
Olfact. Bulbs	79.44	96.60	92.69	67.44
Parafloc	107.72	105.88	100.40	80.54
Resid. brain wt.	96.31	94.34		
% water in brain	99.90	100.28		
Hypophysis	102.02	76.83	96.26	107.06
Thyroids	73.41	70.13	92.66	120.17
Adrenals	83.66	91.12	93.25	52.13
Gonads	91.16	98.34	98.41	82.90

TABLE 7. *Mean values for various measurements in terms of percentage of their corresponding control means for females of hooded, black, and mutant albino strains of rats, to be compared with Wistar albino values (extreme right column)*

Strain	Hooded	Black	Mutant Albino	Wistar Albino
Brain	94.41	98.31	100.25	97.03
Olfact. Bulbs	92.86	112.49	93.03	75.55
Parafloc.	113.07	114.96	101.75	76.34
Resid. brain wt.	100.59	97.59		
% water in brain	99.19	100.06		
Hypophysis	104.21	108.54	101.63	161.20
Thyroids	122.77	54.31	99.51	120.17
Adrenals	86.73	99.22	98.33	67.82
Gonads	92.39	99.27	102.51	77.14

is correlated with their hypoglandular makeup. The effects of single genes are evident in strains synthesized from two mutant coat-character genes. Thus, both the viciousness and hyperglandular constitution are evident in curly R.E.D. and curly hooded rats. The calmness and hypoglandular nature of black is reflected in black hooded and Wistar albino strains. In fact, if we analyze the Wistar albino strain we may see from whence comes at least a part of its modified body and reduced temperament.

Wistar albinos are homozygous for the genes hooded, black, and mutant albino (Table 6). Reduction of Wistar albino brain weight in males is not due to the visible albinism at all, but rather, to the effects of the genes for black and hooded. The Wistar albino male gets its great reduction in olfactory bulbs from all three genes. The enlarged hypophysis of Wistar albino males may be the effect of the hooded gene. The greatly reduced adrenals of Wistar albino males may be the effect of all three genes. The reduced gonads of the

Wistar albino males may be the effect of all three genes, especially hooded.

In the Wistar albino female, just as in the male, we can see from whence come a number of physical modifications underlying their modified behavior (Table 7). Finally, we may say that the Wistar albino rat is to a great extent the quiet, friendly creature that it is because of its reduced brain weight, its reduced olfactory bulbs that cut out much of the disturbing stimuli of the environment, and its reduced adrenals or rage glands. All of these important physical changes result in a large measure from the presence in the Wistar albino of the genes for black and hooded, and to a lesser degree, albinism.

Conclusion

(1) The genes producing certain coat-characters in Norway rats also modify significantly the brain and gland structures of their bodies, and these structural modifications result in modified physiology, which, in turn, produces modified behavior.

(2) Certain effects of individual coat-character genes are evident in the morphology, physiology, and behavior of genetically simple strains bearing one modified gene. Some of these effects appear in synthesized strains built up genetically so as to contain homozygous combinations of two and also of three such coat-character genes.

(3) The behavior effects resulting from brain and gland modifications produced by the genes for black and hooded, and to a lesser extent albino, played a leading role in the original domestication of the laboratory albino rat, although it has probably been selected unwittingly ever since for other unlabeled tameness genes.

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XIV

BLACK MUTANT RATS RAISED IN THE WILD

A burst of huge, vicious, squealing gray rats was flying from a hole in the ground like bullets from a machine gun. They were shooting into a big wire cage that Harvey Clarke had placed over a hole in the ground beside a barn. They were sneezing, cowering, burrowing and forming seething gray masses in the far corners of the cage where they were constantly trying to hide under each other. A few shrieking challenges were exchanged, a few bitter duals fought. Ten- twelve-fifteen and the spectaclar volley of murine projectiles ceased.

"That makes just 2,060 Rattus norvegicus by count that I have caught at this barn in four years," said the professional exterminator as he entered the figures for this last batch in his notebook. "And, of course, an unknown number of others have died in their holes."

The barn of which he spoke was a large, red, wooden structure on the Colony Farm of the Milledgeville State Hospital, located seven miles from town. Mr. Clarke pulled the hose of his cyanide pump from the closed hole in an extensive system of rat tunnels, and knelt down to kill his cageful of rodents.

Through the open end of the cage he inserted a crotched stick with his left hand. He pinned down a rat and cautiously grasped it by the tail with his right hand. Suddenly he yanked the rat out of the cage and dispatched it before it had time to turn upon him.

Each gray rat, when pinned down with the wooden crotch astride its body, became a veritable demon, the epitome of rage: hissing, squealing, laying its ears back, raising the hair along its spine from head to tail, twisting violently and biting the stick ferociously.

"That's strange! It never happened before!" thought Harvey as he immobilized a husky, adult male rat. The rat was obviously afraid, but it showed absolutely none of the well known symptoms of rage or ferocity exhibited by the other 2059 Norway rats he had caught in the vicinity of that barn. Then it dawned upon the exterminator that the rat he was drawing from his cage was black instead of gray.

"Say, maybe this is the black rat the Professor called a mutation. Said when I found one, it would be tame."

That evening, with his wife and children in the car, Mr Clarke drove up to the Georgia State College for Women. He proudly lifted the lid of the luggage compartment and showed me the placid black mutant rat sitting quietly in a box.

We took it to the mouse room of my laboratory to put it in a cage. As we tried to transfer the rat, it escaped and ran around and around the room. At one time we cornered it and actually got it into a cage, but before we could close the cage door, it had slipped out and was racing frantically again. At last both it and we were quite out of breath, but the rat was safely locked in a cylindrical wire cage.

The amazing feature of this rat chase was that at no time did the black rat make a stand. At no time did it defy or attack us. At no time did it raise its dorsal hair or lay its ears back, or chitter with its teeth. Nor did it ever squeal. Once while crossing the laboratory floor, it let out a short, weak "peep".

In the cage the rat sat quietly, and appeared timid. When I dropped food pellets into the cage, it was nervous and disturbed, as would be expected. And when I lowered a dish of water down into the cage within two inches of the rat, it jumped at my bare hand making a strong pushing movement with its paws and hitting my hand with its muzzle -- but it did not bite.

I judged that this remarkably tame black rat, for all of its natural vigor and robust health, would develop a very sore throat and lungs for several days because of the whiff of cyanide gas that it had inhaled, and this turned out to be the case. A day or so later I moved the now wheezing rat to a thick-walled, wooden cage with a shredded paper nest in it. This cage I placed before an electric heater. There the black rat consistently refused to eat pellets of commerical laboratory chow and accepted nothing but bread and milk.

Even with his sore throat and lungs he did not become angry as many rats do during illness, nor did he rush under the nest paper to hide when I lifted the cover from the wooden cage.

Several days later, as soon as his heavy, congested breathing subsided somewhat I put my hand into the cage and ventured to stroke his back. He saw me reach my hand toward him and crouched down a bit, but he never tried to bite.

On the second day that I stroked the rat, he soon backed up a little toward my fingers so that his head would be included with the rest of his body in my stroking. After stroking him for a while, I tried to ease my hand under him to lift him up, but this was too much familiarity to suit him, and, by clicking his teeth three times in the air, he warned me that he had reached the limit of his patience. However, in spite of all this annoyance, he did not attempt to bite.

Next day, after the usual stroking, which he seemed to appreciate, I drew him out by the tail and placed him on my arm. Instead of trying to run away, he insisted on returning quickly to his box and this I permitted.

After a week of captivity we took indoor photographs of the black rat that I held by the tail. He was greatly frightened by the blinding photoflood lights and was almost uncontrollable. He attempted to hide behind my coat lapels and under my arm, but he was not anxious to get away from me. When he did elude my grasp, he merely ran up my arm and sat on the back of my neck. And although quite excited, at no time did he exhibit any anger or viciousness. After two weeks even the photoflood lights did not bother him so much, and after three weeks he would

pose in my hands for pictures. It occurred to me that possibly this tame, black rat had brothers or cousins still alive at the Colony Farm and so after a month Harvey and I went ratting. We smoked out thirty-one rats, two of which, an adult male and an adult female, were tame mutants just like the one we already had in captivity.

The above has been described in detail because, to my knowledge, nobody has ever recorded the remarkably tame behavior of a black mutant Norway rat that grew to adulthood in a wild environment, in competition with its wild and ferocious gray bretheren. And to the student of animal psychology, these reactions during the first few days of captivity are of the greatest interest.

This was not the first time I had observed the phenomen of natural tameness in the black sports of Norway rats, but it was the first time I had examined such sports that had grown up outside a laboratory. Nine years before, Ruth Messer, my assistant, pointed out to me certain black sports appearing in a strain of wild gray Norway rats being raised in our laboratory, and when I studied these animals, I found them to be tame. Other researchers soon corroborated my findings, but the critics contended that the tameness and the blackness were unrelated phenomena and that they only chanced to be associated in the laboratory strains that I examined.

Because I had analyzed the dissection records of many gray Norway rats, and many black sports produced by them, I knew exactly why these sports were tame. First of all, their olfactory bulbs were reduced in size, and hence they could not smell so keenly the dangers in their envionment. Secondly, they had their thyroids so reduced in size that they lived at a quiet tempo. And finally, their adrenals were reduced in size. This prevented their becoming angry at any unusual odor that they did detect.

Obviously, the healthy black rats Harvey Clarke and I captured had something changed in their glands, sense organs or brain, just like my black laboratory sports had years ago, something that made them relatively composed and mild-mannered by nature even in the wild, and obviously this tame tendency is associated with their black coat color. No gray rat showed such tame behavior. Whatever this physiological association in the black rat may be, we do know from my laboratory experiments that both color and behavior trend are inherited, and that the black coat color is simply transmitted from one generation to the next according to the genetic laws of the Moravian monk Gregor Mendel.

But this is not the real reason why the three black mutant rats from the Colony Farm are so important to science. Such tame animals in the wild are really "predomesticated", by their genetic constitutions and all we have to do to create a purebreeding, tame, laboratory strain of rats is to cross together two such "predomesticated" black rats. This is true because the inherent physical modifications producing this tameness are simply inherited. Indeed, there is evidence suggesting that this is exactly the way in which our tame laboratory strains of Norway rats originated in England a little over a century ago. And curiously enough, most of our tame laboratory strains of the Norway rat today are purebred for black, although the rat fanciers, for aesthetic reasons, have added pink-eyed albinism which prevents the black gene from manifesting itself

in the color of the fur coat. Nevertheless, the gland and sense organ changes and the resultant tame behavior tendencies that the black gene brings about are shown very definitely in these same laboratory strains.

Most interesting of all is the fact that Mr. Clarke's tame black rat, sitting peacefully among a cageful of wild and vicious gray rats, demonstrates how "predomestication" trends in behavior, associated with mutant coat colors, may have assisted primitive man in developing his tame animals thousands of years ago. When he selected for breeding, individuals bearing certain mutations that struck his fancy, he was unwittingly but automatically selecting for the natural tameness associated with the altered gene molecule that produced the bizarre color. This gave the domestication process an important boost at the beginning, and we know from actual experiments that the effects of several such behavior-modifying genes is cummulative.

Geneticists recognize that both the color and the tame behavior of the black rat may be due ultimately to a single microscopic gene molecule, or hereditary factor, located in one of the twenty pairs of tiny finger-shaped chromosomes within the nucleus, or central sphere, of all cells within the body of this animal. Such an arrangement is called pleiotropy. Another possibility is that the modified behavior is due ultimately to a different gene from the one that produces the black coat color, and that these two gene molecules reside in the same chromosome or string of genes, because tameness and black color were associated in these animals. This condition is called linkage. So it is a matter either of pleiotrophy or linkage. I favored pleiotropy whereas some of my critics favored linkage.

The exact disposition of this gene or these genes is of great concern to theoretical geneticists and they will argue eruditely about the matter for hours, but to the laymen it makes little difference whether the tameness is produced by the same gene that gives the rat a black coat, or whether tameness and blackness are due to different genes residing in the same gene string.

In my laboratory studies of nearly a decade ago, I had found tameness associated with the black gene in a number of laboratory strains of the Norway rat and I had concluded (against the protest of some) that both black color and tameness are due to the same gene. If mine was the true explanation we could predict that anytime one should find a black mutant rat of this sort among wild gray rats, that mutant rat would tend to be tame, as all three of our black mutant rats from the Colony Farm turned out to be.

We may say also that the occurrence of the tame tendency in these three black mutant rats and never in any of the 2088 gray Norway rats of this population is partial proof of my contention, for the simple reason that single mutations or chemical changes in gene molecules, occur very rarely, and consequently the mutation of two genes simultaneously in the same individual is almost out of the range of statistical probability. Moreover, the repeated, simultaneous mutation of the same two genes first in original laboratory stocks, then in the mutations that occurred in our laboratory, and finally in the mutants at the Colony Farm is virtually impossible.

XV

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COAT COLOR, PHYSIQUE, AND TEMPERAMENT

Materials for the Synthesis of Hereditary Behavior Trends in the Lower Mammals and Man

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IN a number of contributions the author and his associates have shown that certain genes markedly affecting coat color additionally manifest themselves in all parts of the mammalian organism by producing modifications of morphology. Furthermore these coat-color mutations in some instances modify physiological natures, and condition the expression of unique trends in behavior.

Elsewhere we have represented diagramatically the effects of a single gene upon various developmental reactions by means of the branching of a tree of consecutive chains of reaction. The tips of the twigs symbolize the completion of physical development, that is, the fully developed organs with which the Norway rat, for example, carries on the business of life.

The hypothesized mechanism of relationship between a mutant coat color gene and its correlated modifications of morphology, physiology and behavior is illustrated for the male cinnamon rat in Figure 1.

The ontogenetic mechanism which translates gene-potentials into adult form-and-function is much more complicated than this because we know that all physical characteristics are affected by numerous genes. Many of these genes (possibly most of them) interact with each other. We may improve our picture by saying that total development is somewhat like a dense jungle of interwoven trees of reaction, extending from many genes at the ground level to the topmost jungle of branches and twigs in the completed organs. If we imagine the trunk and branches of one tree in this jungle of reactions to be changed to

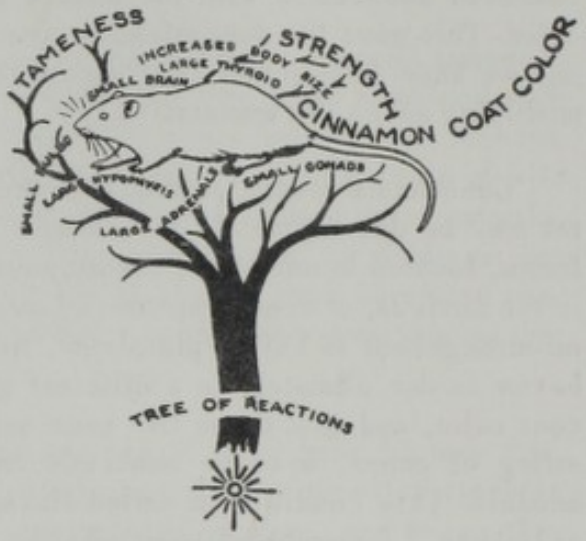


Figure 1

This "tree of reactions" shows the modifications found to be correlated with the presence of the cinnamon gene in the Norway rat. The total developmental mechanism would be represented by a dense jungle of many such "trees," intricately interlaced.

bright yellow (or some other contrasted color) rather than the usual drab brown, we get a better idea of the reactions that are changed by the mutant gene, because the mutant gene expresses itself, naturally, only in the presence of all the other genes essential to the development of the organism.

According to this view, the mutated or altered gene initiates a complex series of altered biochemical reactions, these reactions setting off still other altered reactions, and so on.

An altered hereditary factor or gene produces its altered developmental reactions throughout the whole body of the animal, altering slightly such things as body size, relative proportions of bodily parts, glands, sense organs, brain and hair color. Some of these struc-

tural changes, in turn, modify physiology and the modified physiology produces altered behavior trends some of which are measurable.

If one removes the mutant hair color genetically, (i.e., by substituting some allele), one automatically lifts out the whole tree of associated reactions and effects, including the mutant gene that caused them.

Granting that the above is a reasonably accurate description of the process, if the experimenter, by means of the coat-color handle, lifts out several trees of altered gene reactions, he may combine them together by means of genetic techniques in order to synthesize new, combinational trends in morphology, physiology, and behavior.

In the coat-character-behavior correlations we have a method of determining, directing, or biasing the behavior of individuals in response to their environment. Because the physical basis for such biases is simply inherited it may be compounded by adding together different mutant coat-character genes, which gene complexes may be made by selection to characterize, in turn, whole strains of animals. This mechanism gives into our hands the power to direct the evolution of the behavior of mammalian species, even including man.

I have shown that it is possible to synthesize extremely different behavior patterns in rats by combining two or three mutant coat-character genes, each having small specific effects on morphology, physiology, and behavior.

If the situation represents a general principle, then the Norway rats that we have described previously should not constitute a unique situation. Individuals bearing various mutant coat-character genes among numerous species of mammals should exhibit correlated alterations in morphology, physiology, and behavior.

I announced in 1941 the discovery of a number of morphological, physiological, and behavioristic trends associated with coat character genes in rats, and in 1942 I reported statistical proof of the taming effect of the black non-agouti gene. As was to be expected some prominent biologists were openly skeptical as to the existence of such correlations. One who commended the work said, "I scarcely dare to believe it."

Recently a noted mammalogist suggested that "perhaps these reputations are in the category of old wives tales." Even one observer, who believed that he saw tameness associated with a coat color, added, "I cannot be sure that one of us did not sell the other the ideas."

Such a stage of general skepticism and justifiable doubt is exactly what was to be expected. Here fruitful lines of scientific investigation often start, and our first duty is to collect and eventually to sift all available isolated reports in order to select the materials most suited for further adequately controlled inquiry. To this end for the past five years I have sought to obtain from unimpeachable sources instances of correlation between coat-characters and morphology, physiology, and behavior. I have been impressed with the fact that it is not the imaginative person who is intrigued by the idea, but rather the careful, keen observer, who can describe particular cases. The more superficial person usually dismisses the question with "Never heard of such a thing!" Much of the following list of cases must of necessity be anecdotal, and unless otherwise stated, each story is contained in a personal communication to the author.

Albinos in General

Mr. E. P. Walker, assistant director of the Washington Zoological Park, says, "Albinos are almost invariably such weaklings that I feel sorry to see them exhibited. I have not checked upon the size of albinos but I know that some that I have observed were smaller than the average for their species and I have no doubt that this is generally true."

Horses

The Palamino, buckskin or California golden horse, is noted for its gentle and tractable disposition. A reiteration of this statement has appeared from time to time in farm and country magazines recently. Pedro Martinez, the Tucson cowboy, and other horse trainers agree with this statement.

Martinez tells the story of being in on a project to break a herd of some sixty wild horses. He singled out and lassoed one of the two dappled grays on the ranch. In three days

he was riding this animal to lasso other members of the herd. The other dappled gray had been tamed before his arrival and was being ridden by the ranch owner's young son because of its extreme trustworthiness.

This story fits well with the statement of Major Saunders, as quoted by Robert Cook.[7] "The great popularity of gray horses is apparently well-justified, but I am inclined to wonder if it is the color which made the reputation. Is it not possible that the coat is but the trade mark of a line which transmits good sense and steady conformation?"

Emerson Metoxen, chief of the Turtle Clan, Wisconsin Oneida Indians, tells me that as a boy, he and his comrades used to approach the herd of semi-wild Indian ponies that ranged their reservation, an apple in one hand and a noose of rope in the other. He said that it was most likely to be a palamino, a pinto, or an albino that was bold enough to come forward to get the apple and pay for it with a bareback ride. But should a bay, a dun or a sorrel be caught, the chances were great that the boy would not ride long.

A chief of the Omaha tribe of Indians, reports for the semi-wild Omaha herd of Indian ponies a complete confirmation of Chief Metoxen's account.

E. A. Daubenspeck of Shelby, Montana, reports: "We find that the average run of buckskins, albinos, and poorly bred palaminos are freaks in the literal sense and are generally classed as knotheads in this country."

Members of the Bridle Club of Greensboro, N. C., tell of the stamina of bays, sorrels, and duns in a race, but emphasize the readiness with which blacks loose their "heart" or will to win in a contest of speed. I have heard this elsewhere.

Mrs. Valla Oehme, horse raiser and trainer, tells me that in her many years of experience with horses she finds Palaminos to be very tame and tractable. She finds that dappled grays in general are tame, but that chestnut horses tend to be unruly.

Prof. J. C. Bonner who has "ridden literally hundreds of cavalry horses" tells me that in his experience chestnuts are of unruly temperament, and that the blacks he has handled outside of the service tended to be slow and docile.

Mr. W. S. Kinney, horse trainer and dealer, says that buckskins caught on the range are slow and that dappled gray horses caught on the range are gentle and easy both to break and handle.

Some fifteen years ago a history of the west described how settlers used to single out and catch canyon horses bearing yellow fetlocks, because they could be tamed more readily than the others.

Darwin stated that Paraguayan horses, presumably with curly coat, had "mule feet," meaning, I suppose, feet of abnormally small relative size. I have seen a report stating that these animals are smaller than straight haired horses.

Cattle

An Oklahoma rancher relates how he bought a herd of sixty head of pedigreed Durham cattle in Virginia. Forty-five were brindled, but fifteen were black sports that had cropped out, their appearance being the reason why their wealthy breeder disposed of them. After a year on the range, the newcomer and his associates rounded them up to brand the calves, only to find that the brindled individuals had become so wild that they would attack a man on a horse. Such ferocity he had never observed in cattle before. But the black sports had remained so tame that one could dismount and pat them on the face like dairy cattle. A black cow would charge only when her calf was lassoed and thrown for branding.

Prof. M. B. Rodriguez reports that the small, black Spanish cattle of the Mexican bull fights are very tame until they are "trained" for the arena.

Prof. Wm. A. Richards says that if not confined, black Aberdeen Angus cattle in North Carolina are very tame as compared with brindled Durham cattle.

Probably related to Prof. Richards' account is that of the Argentine Ministry of Agriculture which reports that in comparison with Shorthorn and Hereford Cattle, the temperament of Aberdeen Angus is more active and they possess a greater irritability, facts which are accentuated when they graze in the fields and mountains. Whether this has anything to do with coat color is not known.

Dr. Joequin A. Cortez G., chief of the Department for the Promotion of Livestock Production (Fomento de la Produccion Pecuaria) of the Peruvian Government writes:

"The greatest power of reflecting back heat rays is possessed by the basic color red, which, above all, transforms into terminal energy the radiations of light of the color spectrum. On the basis of this fact the undersigned proceeds to interpret shortly—technically—a practical observation carried out in the year 1936, in the Departamento de Piura, during which a powerful illumination resulted in a temperature above normal, which was accompanied by a prolonged drought. These factors brought about an extraordinary mortality of cattle possessed by many ranches in this province. Without doubt, in certain localities, it was possible to observe that all the animals that were able to survive the action of these unusual phenomena, primarily excessive light and heat, possessed the basic color red."

My great-grandfather, Samuel Rowley, a western Pennsylvania colonist, told my father that he would never have a white or a black ox because their skin was thin and for this reason they would gall readily on the shoulders under the yoke. He preferred brindle, red, or Jersey colored oxen, that had thick skins.

Mr. J. W. Higgins, who helped his father in his business of clearing the virgin woodland of northwest Ohio, said that his father only saved for oxen calves of much the same colors as Samuel Rowley chose, but he never inquired why the selection was made.

Prof. J. C. Bonner, who as a boy snaked logs with an ox team in south Georgia, corroborates this observation so far as his oxen were concerned. He had a red and a black yolked together. The black was thin skinned and was always becoming galled.

The research laboratory of Armour and Company, Chicago meat packers, was approached as to the thinness of skin in black and piebald cattle. Their chief skinner replied that blacks and piebalds have thin skins compared with cattle of other hair colors.

An agricultural report from the Union of South Africa noted that the white areas of piebald cattle broke out in a rash when they ate certain plants. The same was reported for piebald guinea pigs.

O'Flaherty and Roddy[32] reported that when cattle hairs are treated with lime-sodium sulfide solution, crenation and then destruction occurs first in red hair, next in black hair and lastly in white hair both in samples from living animals and from green salted hides.

Darwin states that white cattle are more injured by flies than other colors are.

Sheep

The sensitivity of piebald cattle to certain herbs recalls the work of Heutzinger, referred to by Darwin, that told of white sheep being injured by the eating of certain herbs, whereas the colored animals showed no ill effects.

Swine

In the *Origin of Species* Darwin quotes Heutzinger's finding that white pigs as well as the white sheep mentioned above are injured by the eating of certain plants, whereas the dark-colored individuals escape.

This story fits well with the account that Prof. Jeffries Wyman wrote to Darwin, to the effect that in Florida pigs ate the paint-root (*Lachnanthes*) which colored their bones pink and which caused the hooves of all but the black varieties to drop off. In this fashion, it came about that the pigs of the Florida squatters were black.

In *Plants and Animals under Domestication*, Darwin refers to the better survival of black pigs in Virginia, and that white pigs are more readily affected by the sun.

Otto Mohr quotes the work of Ossent showing that the wild agouti coated swine are relatively immune to *Bacillus suisepticus*, whereas other colors are killed by the disease.

Dogs

A life-long trainer of dogs, Mr. H. R. Watson, says that in his experience, red cocker spaniels are more nervous and noisy than blacks.

I would concur with Mr. Watson's observations and add that I have collected some data to show that reds are more likely to be thin boned and lighter bodied than blacks.

Various fanciers have pointed out to me that black cockers are more likely to have a thick coat and more perfect feathering than are reds born in the same litter. One fancier says this difference in thickness of the coat is the reason for the popularity of red cockers in Georgia, since they are more likely to survive the summer heat.

I have noted the great difference in hair growth impetus between white areas and black spots especially on the sides and hind legs of piebald Spaniels. The white areas will often grow thin, short hair whereas the black spots will develop thick, long hair.

Dr. A. J. Lee, of England, tells me of the "weedy" constitution of chocolate colored Irish terriers.

Darwin says that white terriers suffer from distemper.

It is well known that white bull terriers with blue eyes are likely to be deaf. If the one eye is brown and the other blue, the animal may be deaf only on the blue-eyed side. The inner ear of the deaf side will be found to consist of an unorganized mass of black pigment.

Dr. Taku Komai tells me that "Breeders of the Japanese native dogs state that white dogs are decidedly more tame and often with a defective sense (e.g. deaf or imbecile)—as a matter of fact in old Japan, the white dogs are sometimes thought to be a reincarnation of a human being!, whereas the black or brown ones are more agile and courageous."

Dr. J. M. Phillips reports on cockers "Dilute livers and blacks have very brittle hair so that they look like mangy specimens with bare patches of skin visible by the time they are six months old, while dilute reds may have fair coats.

Blue Merle Collies are smaller than normal."

Foxes

Mr. E. P. Walker believes that in the early days of the silver fox industry, the silver strains then known tended to be wilder than the reds from which they were derived.

Mr. W. Whittingham, who has tried out all the known strains of Silvers, says that one strain will not offer to bite when picked up.

Prof. Joseph Peary says that a strain of Platinum foxes is very tame.

Cats

A case completely analogous to that of deafness of blue-eyed white bull terriers is found in white cats.

C. H. Danforth writes: "I am inclined to think that we have had more wild cats which were agouti, although some of the tamest ones have been agouti. We have had some very wild ones which carried the gene for dilution." However, it must be pointed out that these animals are random specimens and not many of them closely related.

Various zoo keepers, and professional trappers, attest to the greater savageness of the black leopard.

Mr. E. P. Walker says, "I am inclined to believe that black jaguars and black leopards are perhaps slightly less tractable than the normally colored ones."

Squirrels

Mr. Walker writes, "It appears to me that black squirrels are generally dominant in a group."

Clark and Jellison described[6] the tame behavior of pale ground squirrels (*Citellus elegans*). Fichter and Davis[12] review this work as follows: "They observed these pale squirrels, which they considered as mutants, as being more tractable than the normal colored specimens immediately after capture, and quite docile after a short confinement." They continue, "It is of interest to note that the pale specimen of *Citellus elegans tridecemlineatus* (of Fichter and Davis) has been at all times tractable, readily submitting to handling whereas her two sisters have exhibited unpredictable dispositions, even being aggressively pugnacious."

A letter from Fichter states: "'Blondie,' as the pale ground squirrel has been affectionately known for 3 years, was at all times tractable. She was not without temperament, however, often asserting herself with growling, threatening gestures with the front feet, and when being handled, with shoving motions of the muzzle against one's hand or fingers. She never attempted to bite. Her normal colored sister, while offered the same treatment, would never submit to handling. Blondie would climb the side of her cage upon one's approach, expecting to be handed some morsel of food."

Raccoon

I visited a color phase raccoon farm near Bucyrus, Ohio, a number of years ago and observed the notably poorer quality of stiff albino fur. Blacks appeared to have thinner fur than the grays, cinnamons and pink-eyed buffs. A questionnaire was sent to a list of Pennsylvania raccoon breeders in 1942 asking if they had noted any difference in behavior between grays and blacks. A few noted no difference, but the majority said that blacks were tamer than grays (nobody thought the opposite), that they were easier to tame than the grays, and that when once tamed and allowed their freedom about the farm house yard the blacks less frequently than grays returned to the woods.

Mink

A letter in 1942 to Charles Whitaker, an originator of platinum mink, brought the answer that from the beginning they were tamer than the normal colored mink from which they were derived.

Mr. Larry Moore writes, "In regard to the tameness of our mutation mink, I feel that the recessive mutations are tamer than our normal mink. However, I feel that the dominant mutations are of about the same nervous tendency as our dark mink. The blond or Royal Pastel mink are probably the most gentle of them all. We feel that when you cross the dominant and recessive and get what we call the Breath of Spring Silverblu, from breeding a Silverblu to a Blufrost second generation, that this animal is not as tame as the Silverblu recessive, but is possibly a little more gentle than the Blufrost dominant."

In 1946, Mr. Whitaker confirmed the observations of Mr. Moore on all mutant mink varieties.

Mr. W. Whittingham, originator of one strain of Platinum mink by mutation, has this to say: "The Platinum mink is tamer than the dark. We have two that we can carry and we have never had a dark mink that way. The females are the same. They do not exercise like the darks, so get fat and do not produce unless they are cut on feed. Our albinos are like the Plats, maybe not as gentle but not like the darks. And the Pastels are not as wild as the darks. The three strains or mutations are all recessive: Plats, Albinos and Pastels. The dominant Black Cross and Bluefrost are like the darks."

On the contrary, B. C. Backus, of Ward's Natural Science Establishment, tells me that in contrast with eastern mink, normal black Yukon mink tend to fatten and become sluggish unless their diet is watched carefully. He blames the docility of Platinums on Yukon ancestry and the viciousness of Blackcross mutants on excitable eastern ancestry. Thus, it will require a carefully conducted genetic experiment in order to determine whether or not these temperament differences observed in mutant mink are due to coat-color genes or to genes in the residual hereditary backgrounds of the animals, or to both. Mr. Backus' belief is not confirmed by the experience of Mr. Whittingham.

Peromyscus

Frank Clark reported the tame tendencies on the part of pink-eyed dilute *Peromyscus*.

Elizabeth Barto believes that ivory and silver *Peromyscus* on the whole are tamer and more lethargic than those with the wild-type coat color. Her recollection of the first pink-eye dilute mutation is that it was very docile.

R. R. Heustis says that he concurs in Miss Barto's estimates.

Rabbits

W. E. Castle has pointed out that greater size is associated with the chocolate gene in rabbits. It seems probable that size correlations will be found associated with other coat color genes.

More than twenty years ago, when I was a student assistant helping Dr. Castle weigh rabbits, certain individuals of the Vienna White strain used to suffer from epileptic fits, being stimulated apparently by the up and down mo-

tion of the scales. Today I have indications which suggest that the epilepsy be a manifestation of the Vienna White gene, occurring in about 10 per cent of segregating white individuals having one or both eyes blue.

Rats

Castle noted the greater size tendency associated with the chocolate (cinnamon) and the size-reducing tendency of blue gene in the Norway rat, *Rattus norvegicus*.

I have pointed out that in rats a tendency to weight-increase is associated with the cinnamon gene in both males and females and that a similar effect is associated with the curly gene in males, possibly also in females. Weight-decreasing effects were found in both male and female hooded rats, both male and female albinos, as well as in ruby eyed dilutes (both males and females). The interactions of these size tendencies have been described. Similar correlations were found for body length.

Other changes associated with coat-character genes in rats involved tail, testes, thyroid, pituitary, adrenals, femora, olfactory bulbs and nasal bones, brain weight, rate of natural water loss in bones and brain, possibly size and shape of foramen magnum, general activity, basal metabolism, heart rate, voice components, propensity for chewing wood, choice of diet and muscle tonus.

Farris and Yeakel[10] have confirmed the taming effect of the black (non-agouti) gene.

Dr. Komai informs me, "Those who have made a large collection of house rats [in Japan] unanimously assure that the piebald mutants, of which there are a few among thousands, are invariably more docile than the wild types. It is not clear, however, whether they are descendants of a white rat or entire new mutants."

Mice

Castle says of pink-eye, "Certain pink-eyed individuals have been noted in my records as 'jumpers,' because they refuse to remain quiet on the weighing scales long enough for one to observe their weight. Frequently they would turn back-somersaults and then scurry away to a corner of the room. I have never observed comparable behavior among dark-eyed litter mates of such pink-eyed jumpers."

I have noticed this nervous reaction in pink-eye mice, as well as "head weaving." These behavior traits are so marked that they must have been noticed by many other workers.

Feldman,[11] Green,[15,16] Castle *et alii*,[4] have all in turn noted the association of greater size with the chocolate (cinnamon) gene in mice. Castle *et alii* noted the growth promoter tendency associated with the short ear and pink-eye, genes.

Danforth reported the tendency to fatness in lethal yellow mice and Castle showed that their bone structure is increased in size.

I tested several litters segregating for normal and wavy hair form. The wavy animals were of smaller size.

In other experiments, I found an association between a principal silver gene and also the lethal yellow gene with the laying on of fat. One should mention the association of the dominant white gene with lethal anemia and a belly spot with infantile anemia.

Paula Hertwig discovered an association between a crippled leg condition and a hair dilution that she induced with x-rays.

Doubtless a large number of other correlations are known to persons handling inbred strains of mice segregating for coat colors.

Man

Fölling showed me in Oslo some of the phenylpyruvic idiot patients from whom he had described the disease. The associated blond hair may be in part due to the action of the sunlight, and so may not be considered as a natural end stage in pigment development. On one idiot of the Oslo group I noticed that the hair was dark for about a millimeter at the scalp end.

Various reports record the abnormally high rate of tuberculosis in Venetian blonds.[2] I have found confirmation of this in a sample of college students. Venetian blonds do not tend to freckle as do blue-eyed reds.

Many persons believe that red headed persons are more highstrung than the average, but so far as I am aware, convincing evidence has not been presented to date. One member of a family having numerous red headed members says that the reds have little resistance to disease, especially pneumonia.

Flesh and Rothman have reported the finding of a special iron compound in human red hair which they have named trichosiderin. This work suggests a new pigmentation series of reactions aside from the brown-black series.

Dr. Virginia Apgar, Director of Anaesthesia at the Presbyterian Hospital in New York City, says of red heads:

"Due to their thinner skin or to the diminished pigmentation of the skin, these patients show color changes much more vividly than usual. For example, in the head down position or after an ample dose of scopalamine, their skin appears to be bright red while on the other hand, any degree of oxygen lack will make their skin appear remarkably cyanotic: it is possible that a more ample supply of skin capillaries contributes to this observation, a fact supported by the observation that there is more bleeding from the skin when an incision is made. It is also our impression that these patients exhibit vasometer instability to a marked degree for which we have no explanation."

Dr. Paul M. Wood, Secretary-Treasurer of the American Board of Anaesthesiology, writes, ". . . in twenty-two years of personal experience I have discovered that many difficulties have occurred with persons who have red hair. They do not seem to take anaes-

thetics in the same way that others do. Most of them are much more sensitive to the anaesthetic."

Dr. David M. Levy states that red headed persons in general go under anaesthetic more readily than do persons of other pigmentations.

Dr. Marco Nunez confirms these observations that red heads are affected more readily than are other persons.

There are reports in the medical literature to the effect that blonds are less efficient in their use of vitamin A than are brunettes.

J. Grieve finds in man that "there seems to be a small but definite relationship between defective color-vision and dark pigmentation of the iris."

Cyril Burt says, "increased frequency of color-deficiency among dark-eyed groups is fully significant."

Conclusion

There are already enough cases of correlation known between hair characters and morphological, physiological and behavioristic trends, to make worth while the singling out, for detailed study, of specific trees of interrelated morphological, physiological and behavioristic phenomena in the lower mammals and man.

These studies should lead to the synthesis of complex behavior trends in both mammals and man by the employment of the coat-character handle technique described above.

It is hoped that this account will stimulate others to place on record additional coat-character behavior observations and to undertake the synthesis and study of genetic behavior trends.

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CLYDE E. KEELER: The genetic synthesis of behavior trends.

From the beginning of vertebrate genetics it has been realized that certain striking behavior patterns are inherited as mendelian units, for example, tumblers in pigeons and waltzers in mice. Later it was seen that behavior patterns may accompany coat colors, for example, epileptoid fits in Vienna White rabbits, tameness in black Norway rat mutants, nervous behavior in varitint waddler mice, and head turning in chocolate (pastel) mink. Finally, it became apparent that physical modifications, physiological changes and behavioristic trends may be associated together as the results of the tree of altered reactions stemming from a single mutant coat color gene.

We have shown that it is possible to combine such trees of reaction simply by using the coat color manifestation as a marker for a whole tree of alterations. In this way it is possible to augment or negate certain trends on the physical, physiological and behavioristic levels by choosing the requisite trees of altered reaction.

A study of brain and glandular modifications of black, hooded and albino rats shows that the laboratory albino rat (containing these three genes) is to a large extent tamed by the additive taming effects of the genes for black, hooded and albino.

A survey of possible mammalian materials suggested that the recently cultured fissiped carnivore species *Mustela vison* abounds in gene mutations affecting the color of the coat and also in temperament and behavior alterations some of which appear to be associated with coat color mutations.

With the idea of extending the rodent observations and experimental synthesis to mink, a joint research project has been undertaken with Mr. LARRY MOORE. Mr. MOORE has obtained photoelectric cell records of the activity of several strains of mink in their cages, which records will be published in the future. Suffice is to say here, that degree of activity (which is correlated with degree of viciousness), is great for Dark mink, Black Cross (formerly Royal Kohinur) and Blufrost. Pastel and Silverblu are inactive and relatively tame.

Since thyroid activity appears unable to explain the physical activity and temperament alterations of coat color mutant rats, since large adrenal size relative to body size was found associated with vicious temperament in rats and since small adrenal size was found associated with docile temperament in rats, it was decided to test the adrenal-body weight ratio in the above mentioned strains of mink.

The present author dissected 775 carcasses of mink raised by Mr. MOORE. We shall publish details of this work in the future, but the adrenal-body weight findings may be referred to here.

It has been observed that the size of adrenal per unit of body weight in both sexes of relatively tame Silverblu mink is significantly smaller than that of Dark mink. The same is true of relatively tame Pastel mink. Wild and vicious tempered Blufrost and Black Cross mink have relatively large adrenals per unit of body weight resembling the condition in wild and vicious normal Dark mink.

We have shown that Pastel and Silverblu mink are significantly larger than normal Dark mink and that Blufrost and Royal Kohinur are significantly smaller than normal Dark mink. It is known that children have relatively large adrenals whereas adult human beings have relatively small adrenals. In view of these facts we thought that we might be dealing with heterogonic growth of the adrenals in colorphase mink, possibly induced by an altered pituitary that changes body size primarily. Further consideration of our data shows that this is not the case.

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XVII

CORRELATIONS OF MORPHOLOGY, PHYSIOLOGY AND BEHAVIOR WITH HEREDITARY COAT COLOR VARIATIONS OF MAMMALS

By Clyde E. KEELER (Milledgeville, Georgia, U. S. A.)

In a number of contributions since 1941 my associates and I have published data proving that certain coat color genes release a whole tree of modified developmental reactions leading eventually to many significant but previously unsuspected alterations of morphology, physiology and behavior.

Typical of these many trees of modification stemming from single coat color genes is that released by the cinnamon gene of the Norway rat (*Rattus norvegicus*). This gene not only produces a brown color of the coat, but tends also to determine smaller gonads, larger adrenals (but probably smaller per body weight), larger hypophysis, larger thyroids, smaller olfactory bulbs, smaller brain, larger body size, great strength, and marked tameness.

An observational survey of mammalian species suggests that similar modifications are correlated with coat color genes in horses, cattle, swine, dogs foxes, cats, squirrels, raccoon, mink, Peromyscus, rabbits, rats, house mice and man.

We have singled out Pastel, Silverblu, Black Cross (formerly Kohinur) and Blufrost coat color mutants of the mink (*Mustela vison*) for particular study. Larry Moore and I have found that Silverblu and Pastel mink are significantly larger than their normal Dark mink controls. We found that Black Cross and Blufrost are significantly smaller than their controls.

We measured relative activity of the different strains by means of photoelectric cells found both Silverblu and Pastel to be relatively inactive whereas Black Cross and Blufrost are almost as active as Dark mink. Savageness is directly correlated with activity. These results are unpublished.

Finally, from a series of 775 dissections, we selected adrenal and body weight data upon the four mutant strains in question as well as for their Dark controls. We compared the ratio of adrenal weight to body weight of each mutant strain with the corresponding ratio of the Dark controls. The tame, large and relatively inactive Pastel and Silverblu animals have significantly less adrenal gland per unit of body weight than the normal Dark mink. The savage, small and relatively active Black Cross and Blufrost animals, although actually having slightly less adrenal per unit of body weight in our sample, do not differ significantly from their normal Dark controls.

Because we have shown previously in the rat that the reduction of adrenals made by single coat color genes is additive when these genes are combined in the same individuals, it should be possible by combining such taming genes as Pastel and Silverblu to produce completely tame strains of mink and other wild mammals.

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THE MINUTE STRUCTURE OF HAIR AND CORRELATIONS WITH MORPHOLOGY, PHYSIOLOGY AND BEHAVIOR[1]

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The hair of mammals varies greatly in its minute structure among individuals of those species that have been studied adequately. Thus, we have short-haired "rex" types with curly vibrissae in the rabbit, rat, mouse, pig and horse. We note almost hairless types in rat, mouse, dog and sheep. We see numerous piebald types in many mammals. Chinchilla forms are found in mouse, cat, and rabbit. Albinos are present in many species. We observe in several mammals: chocolate, blue, yellow, black and pink-eyed buff forms. When individual hairs from the color mutants are examined under a microscope, the colors turn out to be due to variations in quantity, quality and distribution of pigment granules in the hair.



Fig. 1. Adult male black sport of the Norway rat caught at the colony farm.

Gruneberg (1943) suggests that the pigments of mouse hair consist of yellow phaeomelanins which are easily dissolved in alkali, and dark eumelanins which are very resistant to alkali. He suggests that black and brown pigments differ only in particle size. Dunn and

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Einsele (1938), showed that darker forms have larger pigment granules than lighter forms. Daniel (1938), from spectroscopic studies, concluded that albino gene-combinations with black or brown are very similar, if not identical, and hence presumbably of the same chemical constitution. In yellow mice, according to Dry (1928), black pigment is reduced to a few scattered granules, leaving the fur bright yellow or orange. White-bellied agoutis have dorsal hairs showing a darkly pigmented base containing black and brown granules, a subterminal band of yellow, and a black tip. This is like the fur of many wild mammals. Werneke (1916), reported the pigment of pink-eyed dilute mice to be reduced not only in amount, but also that it occurs in granules of less regular shape than normal. Onslow (1915), corroborated by Charles (1938), showed that the white-furred areas of piebald mice and Dutch rabbits are unpigmented because they lack the enzyme (tyrosinase of Onslow, dopa-oxidose of Bloch).

Because many of these microscopic conditions are distinguishable to the human eye, and most of them appear as differences in color, texture or form, it will be simpler for purposes of this paper to speak of them in visual terms. Thus, when we discuss various coat colors in mammals, we must keep in mind that these color terms usually refer to quantity, quality, and distribution of melanin pigment granules within the hair.

The subject of correlations in morphology, physiology and behavior associated with distinct types of melanic pigment development in dermal appendages is not entirely new. It merely has been neglected. For many years white cats or white English bull terriers with blue eyes have been known to tend toward deafness. Darwin (1890) in his chapter on correlated variability, noted such cases and also quoted Professor Wyman to the effect that in Virginia all hogs except black ones suffered from eating the root of *Lachnanthes tinctoria*. Spinola is quoted as stating that *Polygonum fagopyrum* (buckwheat) is injurious to white and spotted pigs in the sunshine, but not to black pigs. Other cases are cited by Darwin. Castle (1941), and his students had found certain coat colors to be associated with size in rats, mice and rabbits.

In 1941 my assistant, Miss Ruth Meeser, pointed out to me certain adult black sports appearing in a strain of wild and savage, gray Norway rats being raised in our laboratory, and upon examination I found them to be tame and docile (Keeler, 1942). Biologists know very well that it is almost impossible to tame adult, Norway rats and the remarkable change in behavior exhibited by our black sports required an explanation. Other coat color variations occurring in this same strain of Norway rats were found to be slightly modified in behavior. Some of these, such as chocolate, piebald and pink eye were in the direction of tameness. The curly rats were extremely wild and savage in their cages but once captured and removed from the cage, they sat quiet and subdued.

Correlation of Hair Structure with Other Characters

A physical basis for these behavior phenomena was sought in Dr. H. H. Donaldson's voluminous records of meticulous dissections carried out mainly by Miss Meeser over a period of many years. (Keeler and King, 1942). We will not review this work in detail here but will merely refer to certain morphological changes in the black sports. The black sports were of less than average body size (Keeler, 1947*a*), and had thyroids, gonads, adrenals, olfactory bulbs and brain, distinctly smaller (Keeler, 1947*b*) than those of their gray Norway controls. The reduced thyroids and gonads caused them to live at a more quiet tempo (Shopbach *et al.*). The reduced olfactory bulbs allowed the mutant blacks to sense fewer of the dangers in the environment, and the reduced adrenals kept them from becoming excited and angry about the little that they did smell. Tests with garlic (Keeler, 1942), which rats hate, showed the blacks to be less affected than are gray rats. They did not react to the presence of strangers until they stood in front of their cages whereas the grays huddled together in the far corners of their cages when strangers entered the door forty feet away. There is evidence that most coat-color mutant rats spin through their life processes at a much more rapid rate than do the gray controls, as measured by the rate of water loss in bones (Keeler, 1946) and other tissues. There is also evidence (unpublished) that the natural length of life is usually reduced in mutants. The reduction of gonads as well as the very slight decrease in body size should affect the voice of the black mutant rat, and certain studies on voice analyzer records indicate that the voice is raised (Keeler, 1945). However, the black sports tend generally to be of a silent, cringing nature, using their voices very little.

The responses of scientists to our correlation studies on black sports have ranged from recognition (Cook, 1941), to scientific doubt. Critics have objected to the fact that our black sports appeared in a stock of wild gray Norway rats being maintained in laboratory cages. Anything could happen in a laboratory, they maintained. Adhering to the "one gene—one function" idea, they denied that the physical modifications of glands, sense organs and brain could possibly be pleiotropic manifestations of the black pigment-producing gene itself, but contended that these alterations must be due to a second mutant gene closely linked on the same chromosome with the black-producing gene. They did concede, however, that if one caught an adult, black sport among wild Gray Norway rats, and if that sport was found to be tame, then this was a case of pleiotropy, as I maintained, rather than one of close linkage, because the simultaneous mutation of the same two linked genes is a highly improbable event.

On January 3, 1950, Harvey Clark, a professional exterminator, brought me the adult, male, black sport of the Norway rat shown in figure 1. The photograph was taken three weeks after capture.

This animal is silent, slow, and cringing. It has never offered to bite. The black sport was caught on the large Colony Farm of the Milledgeville State Hospital seven-and-a-half miles south of town.

A month after its capture the exterminator and I went back to this farm and smoked out two more adult, black mutants, a male and a female—both tame. (A total of 2085 wild and savage Norway rats have been caught at this farm in four years.) If these mutants reproduce, their offspring should constitute a "predomesticated" stock of tame laboratory rats directly out of the wild. The physical modifications of these black sports of the Norway rat must determine quietness and docility within the normal range of behavior as was the case with the mutant blacks of the laboratory.

If we look at other species of mammals, we find a number of cases that appear to be similar. For example, a group of raccoon fanciers reported the black raccoon sport to be docile as compared with the gray (Keeler, 1947*c*). Clarke recorded the pink-eyed Peromyscus to bear tame tendencies, and Barto believes that ivory and silver Peromyscus are tamer and more lethargic than those bearing the wild-type coat color (Keeler, 1947*c*). The Silverblu platinum mutation has occurred twice in mink and both times it was accompanied by tamer behavior than that of the average dark mink (Keeler, 1947*c*). The Snowball mutation of the Cotton rat of Danforth and Schwentker (1949), shows tame tendencies (personal communication). Recently the white-faced mutation of the hamster described by Foote (1949) has been found to be accompanied by increased nervousness (personal communication). In these cases it may be said that the modifications associated with the simply inherited color variations are within the *normal* range of behavior.

In contrast to the above, many cases are known of coat color mutants in which morphology, physiology and behavior are *abnormally* modified. For example, we may mention the varitint-waddler mouse of Cloudman and Bunker (1942), in which a peculiar spotting is always accompanied by palsy. Completely white Vienna White rabbits with blue eyes tend to epileptoid fits when frightened, as Castle and I observed (unpublished) many years ago, and as had been thoroughly studied before World War II by Nachtsheim (1939). It appears, according to Larry Moore and others, that the Aleutian sport, used in the production of Sapphire mink, tends to spontaneous bleeding. Numerous individuals raising Pastel mink have noted the jerky head movements manifested by some individuals. These head movements (screw neck) follow the Pastel gene and appear in any combination of coat colors containing Pastel. A study of this characteristic has been made by Shackleford and Cole (1947). We might mention the case of the dominant white mouse derived from the Manhattan Project and published by Grobman and Charles (1947). One dose of this gene changes a black coat to blue. Two doses makes the animal completely white and usually prevents the

development of its eyeballs. Many blue-eyed white cats and white English bull terriers are deaf. The deaf, white cats were recorded by Darwin (1890) and studied thoroughly by Przibram (1907). The eye and ear abnormalities of surviving purebred Blue Merle Collies and Dunkerhunde might also be mentioned (Hagedoorn, 1946). Many dominant *lethals* are known in mammals associated with coat colors: as yellow and dominant spotting in the mouse (Cuenot, 1908; Ibsen *et al.*, 1917), Blufrost in mink (Moore and Keeler, 1947), and Snowball in the Cotton rat (Danforth *et al.*, 1949). When a single gene for these characteristics is present, the animal is viable, but two genes for these variations will kill every individual that receives them.

My co-workers and I (1949) have been able to prove that morphology, physiology and behavior differences are associated with a variation of the broadbreasted bronze turkey known as "faded feather." Faded feather mutants are smaller and weaker than normal turkey poults at hatching. Their eyes are defective. They are reduced in energy. They remain of smaller size. Their bones are weak and apparently deficient in calcium. They break their wings more frequently than do the normals, and may show green-stick fractures. Their feathers are weak and break readily in all parts, including the barbules. A high percentage of faded toms do not gobble. The mortality of faded feather mutants is 50 percent compared with 10 percent for normal broadbreasted bronze turkeys.

I have extended my observations to the albino mutant of the ring-neck dove *(Streptopelia roseogrisea)* and find the albinos reduced in activity, lacking in energy, and softer in voice than the controls. The albino form is much more easily tamed than the bisque colored birds. In two weeks I had a pair of albinos sitting on my finger, but in four months I have not been able to get a pair of bisque birds to sit on a stick held in my hand. From the literature it is apparent that albinism reduces voluntary activity and softens the voice in mocking birds (McIlhenny, 1940). Darwin (1890) states that the albino Pea-fowl of England and France are smaller than the normal in body size. The albino rice bird of the Japanese fancier is smaller of body, softer of voice and less active than the normal color variety. Mr. Carnochan and Dr. Myron Gordon tell me that the albino form of the Paradise Fish is probably more quiet, and that the males fight less, than is the case with the normally pigmented variety. Thus, the correlations that we have been considering, are not confined to mammals alone, but are characteristic of birds and possibly of fish as well.

At present, I have under observation in my laboratory, the Vienna white rabbit, the Snowball Cotton rat, the white-faced hamster, the black mutant rat, the albino ringneck dove, the Manhattan Project dominant white mouse, and the varitint-waddler mouse, as well as other more widely known mouse variations. If this association of

alterations in morphology, physiology and behavior with color of dermal appendages is true for mammals and birds and possibly for fish, then this is a vertebrate phenomenon and likely to apply to man. But human behavior is so complex that it is difficult to collect incontrovertable data. At present, I am searching for such correlations among human beings. I am confining my studies to albinos and redheads (Keeler, 1947*c*).

There appears to be some reason to suspect that human albinos may be low in basal metabolism and often deficient in energy, as is the case with certain albino birds and mammals. They may possibly be low in blood calcium. They may be deficient in the production of antibodies against various disease germs, thus shortening their average length of life. Red heads are hypersensitive to ether and narcotics and are profuse bleeders at operations. They have a sensitive sympathetic system control of the skin capillaries. They may possibly be more responsive than others to niacin in that they blush more readily after the administration of this vitamin. Some think that they may be more susceptible than the average to pulmonary tuberculosis. It appears that other variations in physiology and behavior may be associated with the exaggerated capillary reactions.

Curiously enough, these probable associations of capillary phenomena with physiology and behavior are in line with the age-old, popular conception of red heads, which may turn out to have some basis in fact. It is desirable that observations be made in this direction, but they must be made on a strictly scientific basis, and this is a rather difficult thing to do. However, such scientific researches are not impossible, and I believe that in the near future they will reveal true associations of morphology, physiology, and behavior associated with natural hair colors in man, as has been demonstrated so abundantly in mammals and also in birds.

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NOTE ON COAT COLOR AND PHYSIOGNOMY IN NORWAY RATS[1]

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Sir Arthur Keith (1922) recognized that the bony structure of the human face may be greatly modified in certain individuals by pituitary hyperactivity (gigantism, acromegaly) and thyroid hypoactivity (achondroplasia, cretinism, mongolism). He also postulated that the tendency toward similarity in shape of face and form of body found in many individuals belonging to the same race are due in a large measure to inherited variations in quantity of the several hormone secretions that go to make up the particular glandular balance most frequently present in individuals of a particular racial group. On this basis of facial features and body form, Keith suggested that Mongolians (as compared with Caucasians) tend to have reduced adrenal, reduced interstitial, reduced pituitary, and reduced thyroid glands. Negroes in general (as compared with Caucasians) have greatly reduced adrenal, reduced interstitial, reduced pituitary, and reduced thyroid. Long legged Nilotic Negroes (as compared with Caucasians) have greatly reduced adrenal, greatly reduced interstitial, reduced pituitary, and reduced thyroid. Pygmies (as compared with Caucasians) have greatly reduced adrenal, reduced interstitial, greatly reduced pituitary, and reduced thyroid.

These racial trends in body development and face shape are very difficult to study statistically and to correlate with measureable glandular function, especially because of the great amount of hereditary variability found in each so-called race of mankind, which variability causes the races to overlap with respect to most characteristics studied. These modal racial types postulated by Keith undoubtedly represent the effects of multiple genetic factors affecting endocrine output in the several glands of internal secretion. Keith's proposition will probably long remain in the form of an "hypothesis" because usually the effects of single genes in a racial complex cannot be identified. For the present, at least, such material is incapable of complete analysis.

Some light may be thrown on the problem of the relationship of glandular function to physiognomy by the study of face shape of specific pigment variants found in human populations. The face shape effects should be particularly recognizable in populations in which the residual hereditary background upon which the effects of the mutant gene are displayed, has been made more homogeneous through inbreeding. Thus, the Moon-child (Keeler, 1950) of the Caribe-Cuna tribe of Indians probably tends toward brachycephaly with underdevelopment of the bony structures about the base of the nose. Part of

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the associated glandular variation appears to be hypothyroidism, but more extensive studies are desirable.

A glance at the products of hybridization of the many recognized breeds of dogs adds evidence for inherited glandular effects on face and body form (Stockard, Anderson, and James, 1941). Here, as in

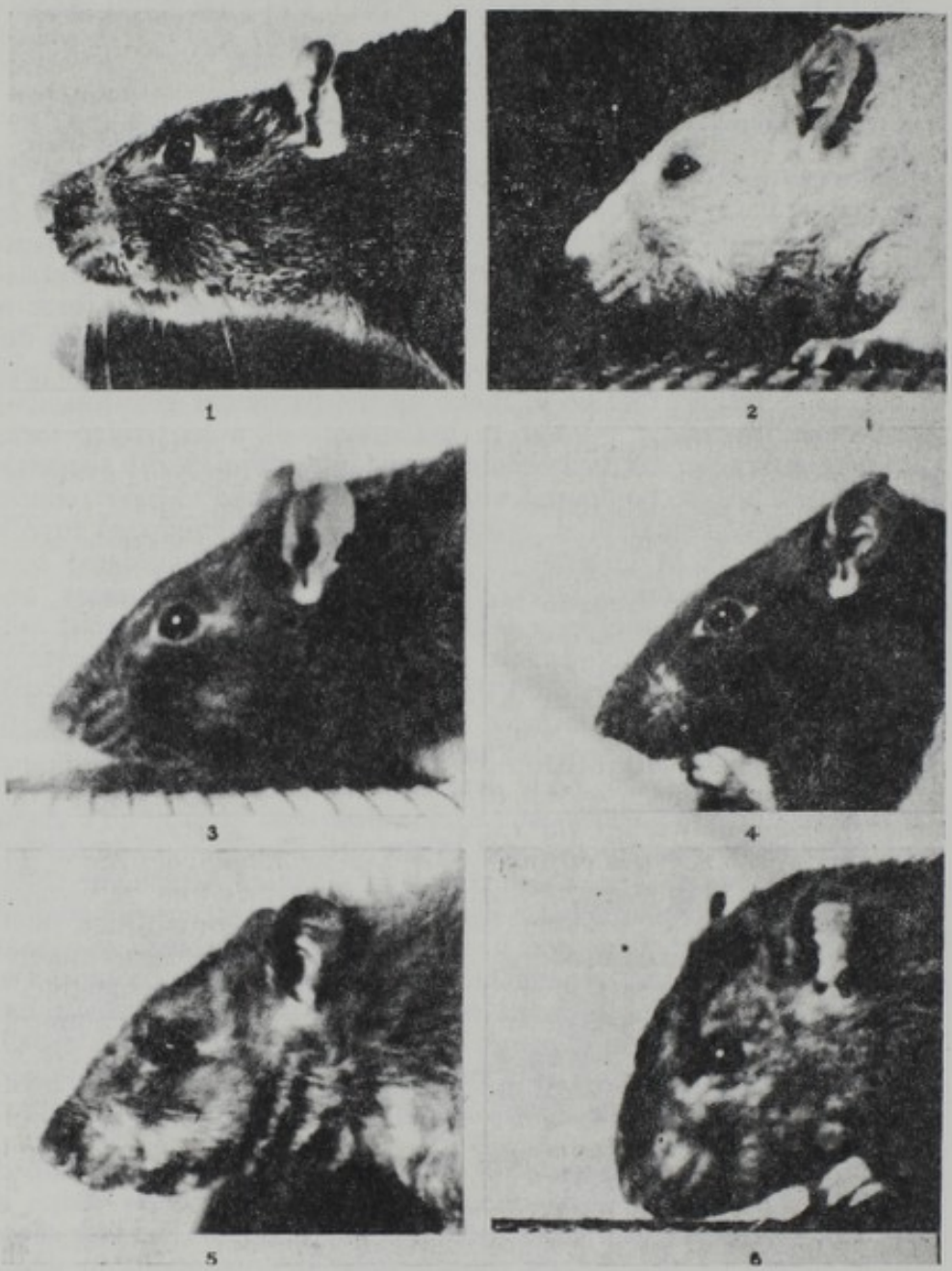


Plate I. Face shapes of various strains of Norway rats from mutations occurring in wild gray laboratory stocks. Tip of nose in figure 1 and leg in figure 3 retouched. Fig. 1, wild gray Norway male. Fig. 2, albino mutant male. Fig. 3, black (non-agouti) mutant male. Fig. 4, male rat bearing a combination of black and hooded (piebald) mutations. Fig. 5, curly haired mutant male. Fig. 6, cinnamon mutant male.

most human cases, we cannot analyze the matter further because we have no labels on the many genetic units that cause the modifications and usually, therefore, we cannot synthesize face shape types at will by making combinations of the monogenetically induced differences in glandular function. However, certain other mammals such as fur foxes, fur mink, and Norway rats may provide more useful experimental materials because specific glandular modifications are among the pleiotropic effects of certain pigment-modifying genes that are simply inherited.

For thirteen years I have been studying the pleiotropic effects of certain coat color genes in the Norway rat. During this period it has become increasingly evident that certain pigment-modifying genes do affect face shape, presumably through the intermediation of the glands of internal secretion that affect development of bony structures locally as well as generally. For this study it is only necessary to observe a strain of wild, gray, Norway rats that is inbred (thus, acquiring a uniform residual hereditary background) and to compare these individuals with those of strains that arise from the gray strain by mutations at single gene loci.

In order not to complicate the study with a consideration of sex differences, I have compared adult males of similar ages. Profile photographs were taken of several mutant strains derived from the inbred wild gray strain. The glandular comparisons between these strains have been considered previously (Keeler, 1947). The wild gray Norway male has a strongly constructed head with powerful jaws and a well built nose, for olfaction is the dominant sense in the wild, gray, Norway rat (Fig. 1). The albino mutant has the nose somewhat reduced and shortened (Fig. 2). The eyes are not prominent and this may indicate thyroid deficiency, although the albino mutant is a plucky and vicious antagonist. The black (non-agouti) mutant has the face pointed with a receding upper lip and jaw (Fig. 3). The olfactory bulbs are greatly reduced in size as is the brain. The eyes are fairly prominent but less so than in the wild gray. As Arthur Cohen says of them, "They look as though you stuck their faces into a pencil sharpener." Black mutants do not compete well with grays in battle. The black-piebalds have long, narrow heads with pointed faces and drooping noses (Fig. 4). Their eyes usually protrude. The curly rat is known to have enlarged thyroids, and as a result, its behavior is nervous and erratic. Its face is pointed (Fig. 5). The jaws appear weakly developed and the eyes pop. The cinnamons tend to become acromegalics with wide heads, massive lower jaws, and relatively small, pop eyes (Fig. 6). The upper lip does not appear to be enlarged. Cinnamons tend to grow larger than wild grays and hence the pituitary is probably hyperactive. Such an overactive pituitary would account for the trend toward acromegaly.

The important thing about this material is that by using coat color and hair form as labels for these several monogenic alterations in glandular function, individuals may be synthesized in which are combined the coat colors and hence the accompanying glandular effects

of several genes. For example, what will be the result in face shape produced by combining curly (hyperthyroid) with albino (hypothyroid)? Or what will be the result of combining cinnamon (hyperpituitary) with black (non-agouti) (hypothyroid, hypointerstitial, hypoadrenal)?

I believe that such Norway rat materials in the hands of competent experimenters over a long period of time can yield much concerning the analysis and the synthesis of specific body types and especially of face shapes.

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XX

THE GEORGIA ACADEMY OF SCIENCE

A PRELIMINARY SURVEY OF VOICE VARIATIONS IN RATS AND THEIR GENE CONTROL

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Persons employing rats for scientific purposes may have observed that individual animals demonstrate distinguishable types of voice according to whether their vocal expression is occasioned by uneasiness, fear or anger, pain and sexual excitement. Female voices can sometimes be distinguished from those of males, and it is always noted how the faint, almost inaudible, high pitched squeak of the suckling rat is gradually transformed into the harsh, terrifying shriek of the mature adult. So far as we are aware, no one has attempted to analyze the "language of the rat," although such a "language" is undoubtedly capable of description.

The voice of the rat probably varies slightly with sex, more with the evoking situation and the most with age. Our studies, here to be described, add gene constitution as a fourth factor controlling audibly distinguishable voice differences in rats.

METHODS AND MATERIALS

In order to eliminate the possible differences due to sex, male rats only have been employed in this survey. To negate so far as possible the effects of age, only mature adults have been tested. That we might provide a uniform evoking stimulus for testing their voices, each animal was caught with a pair of tongs by the skin of the side or back and held suspended before the microphone of a sound prism (Schuck, 1934). If this procedure, which usually proved sufficient, failed to induce a cry, the rat was pinched at the base of the tail with a second pair of rat tongs.

We observe that under presumably the same stimulus of being picked up with forceps, one rat may merely whine a slight protest and make no attempt to escape, whereas another rat may shriek with rage, struggling and biting frantically for several minutes; another may emit a cry as of fear and struggle to escape without biting. We realize that in all future work it will be necessary to devise methods of producing, so far as possible, a uniform evoking stimulus to call forth the outcry. We believe that it is not always possible to elicit an outcry because some dwarfs, for example, could probably be slowly crushed to death without registering their objections vocally.

The test animals for which we obtained successful records belonged to strains as follows: black; pink-eyed yellow; black-eyed yellow; black piebald; all of tame laboratory stock in addition to the late

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Dr. Helen D. King's wild gray Norway stock and its mutant derivative strains of: mutant albino; cinnamon; curly; stub tail. Two combination strains exhibiting two mutations each were investigated, namely: Ruby-eyed curly; and Black Curly.

Voice Characteristics and Recording Equipment

An analysis of the sound wave of a sustained tone, such as might be produced on a vibrating wire or string, shows that it will consist of components of various frequencies. These frequencies are all exact multiples of the lowest frequency present, which is known as the fundamental frequency. The other components are known as harmonics or overtones.

The human ear is sensitive to three general characteristics of sound. They are pitch, intensity, and quality. Pitch is determined by the frequency, high pitch corresponding with high frequency; intensity by the amplitude of vibration; and quality by the harmonic structure (number of components present and their relative amplitudes).

The sound prism used in this study is a device which will analyze a sustained tone giving the frequency and relative amplitudes of all components in one-tenth of a second. Thus a tone need only be sustained for that period of time to be accurately analyzed. However, by using an oscillograph in conjunction with the sound prism, successive analyses may be recorded photographically, so that variations of the sound with time may be noted.

In our experiments the sound wave was picked up by a microphone placed about one foot from the source, amplified, analyzed, and recorded on a rotating film drum, so that approximately fifteen successive analyses were obtained over a period of one and one-half seconds. The frequency range covered all components between 100 and 8,000 cycles per second, and relative amplitudes ranging approximately from 30 to 1 were observed. The accuracy of determining the frequency of any particular component is not better than plus or minus 50 cycles per second.

A preliminary study of our records indicated that it would be advisable to classify them according to (1) variations with time, (2) harmonic structure, and (3) frequency of fundamental.

All records showed variations with time. Some were relative-constant, however, over periods of one-half second or more, and these were placed in the sustained group. Others indicated that the sound existed only long enough to be recorded in one or two successive analyses and these were placed in the transient group. Records of sounds that existed for periods of time longer than several tenths of a second, but which exhibited important changes in frequency or in relative amplitude of the components, were placed in the varying group.

The harmonic structure determines the intensity and quality of the tone. This class was divided into two groups giving (a) the

number of harmonics present, and (b) the number of these harmonics which showed comparatively large amplitudes.

Although the fine details of such analyses are not always distinguishable to the human auditor, in a crude way he may be aware of some of these characteristics in a voice. For example, a simple, high-pitched, clear, whistle voice to the human ear would be found to possess one high fundamental frequency of larger amplitude, in addition to which there might be several harmonics of minor amplitude. The addition of harmonics may "improve" the "tone quality," on the other hand, a harsh raucous sounding cry, unlike a whistle, is more likely to be found transient, or varying. It will probably have a larger number of harmonics than the whistle-voice, but these will usually be of rapidly varying amplitude and frequency. The fundamental frequency may be low. Some of the fundamental frequencies have been placed on their appropriate positions on the diagram of a piano keyboard in figure 1. It will be seen that they are easily distinguishable to the human ear.

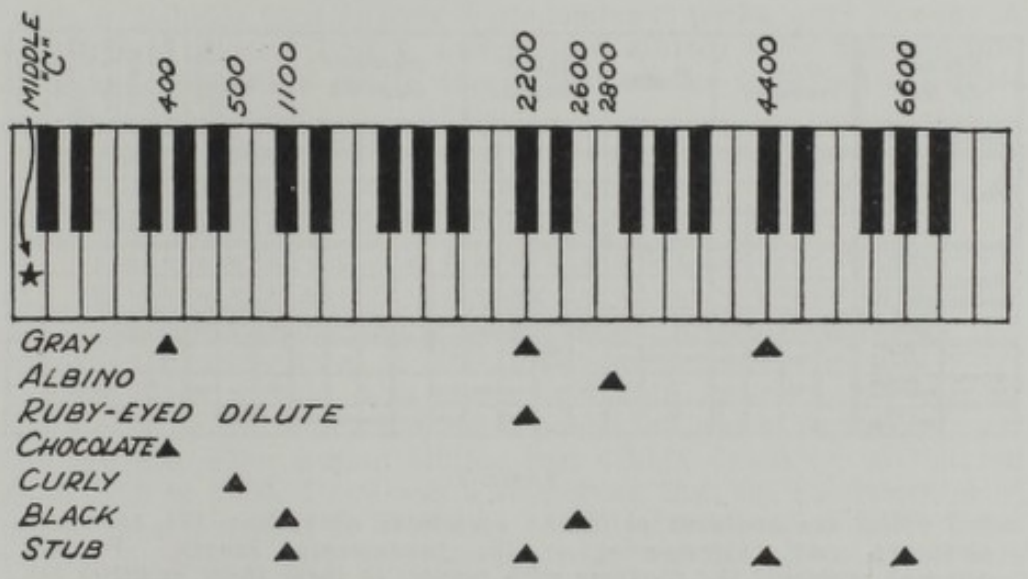


FIGURE 1. *Portion of a piano keyboard above which is indicated the frequency of pitch in vibrations per second. Below the keyboard is indicated by triangles the position of fundamental tone and overtones recorded on the sound prism for adult male rats of several inbred strains described in the text.*

ANALYSIS RECORDS

A number of direct auditory observations had been made upon animals belonging to various strains that had been employed for a study of the pleiotropic effects of coat color genes (Keeler and King, 1942; Keeler, 1947). These observations were as follows:

(1) Gray Norway rats have loud, raucous voices with low pitch.

(2) Curly rats have voices similar to those of gray rats but of less intensity.

(3) Mutant albinos have, in general, a whistle voice of high pitch.

(4) Stub tail rats, although having a voice of less intensity and of less purity of tone than mutant albinos, have a high pitch.

(5) Cinnamon rats have a voice similar to that of gray Norways.

(6) Pink-eyed yellow rats have a medium high pitched voice similar to that of black-eyed yellows.

(7) Black rats have a high pitched voice as do black piebald rats.

(8) Ruby-eyed curly rats have a medium pitched voice.

(9) Black curly rats have a low pitched voice.

Because of the preliminary nature of these observations, it is not to be assumed that they can serve as more than a guide for further work, and possibly they may not even represent accurately average descriptions of the voices of these strains when examined under controlled conditions.

They are, however, corroborated by our analytical check shown in table 1.

Strain of Rat	Gray Norway				Curly			Black Piebald				Mutant Albino					Stub		Pink-Eye Curly	Cinnamon	Black	Ruby-Eye Yellow	Black-Eye Yellow	Black-Curly
Specimen No.	1	2	3	4	1	2	3	1	2	3	4	1	2	3	4	5	1	2	1	1	1	1	1	1
Time		X	X		X	(X)	X		X		X		(X)							X		X	X	X
	X			X	X	(X)		X		X		X	(X)	X	X	X	X	X	X		X			
	X			X	X			X		X							X		X		X			
Harmonic Structure	12	3	3	4	6-12	1	7	3	1	3	3	3	1	3	3	1	3	4	3	3	3	3	7	7
	2	2	2	3	1	1	2	2	1	3	3	1	1	1	1	1	2	1	2	2	2	(3)		1
Frequency of Fundamental																								

Table 1

Rat voices are analyzed as to (1) variations with time, (2) harmonic structure, and (3) frequency of the fundamental length. Vertical columns represent the analyses with respect to these three qualities for a single specimen. Where parentheses are used, there is a question between two alternatives. Under time variations, an X mark indicates presence of a characteristic. Under harmonic structure with respect to number of predominant peaks, the small number (1-3) represents the actual number of such peaks whereas the larger number (1000-6000) represents the value of those peaks in cycles per second.

From a sample of one mature adult male rat from each of the above mentioned strains we first obtained one or more clear analysis records on photographic film. From these we learned that, roughly, auditory impressions do separate gross voice differences.

We selected additional rats of the gray Norway, curly, black piebald, mutant albino, and stub tail strains for further study.

For each of these strains we may obtain voice records from the same individuals which indicate that the voice of a particular rat may be at one time sustained and at another time varying. For a single curly rat (specimen No. 1) we actually obtained records of transient, sustained and varying time quality. This lack of uniformity may be associated with the change of psychological motive, the intensity ot the struggle to become free from the forceps, the tensed muscles of the throat and other physical factors. However, a tendency of the mutant albino voice to be sustained is apparent in our records.

When quality and intensity features of voice are examined, it is found that 12 harmonics are present in the record of one gray Norway rat; 8-12 in a curly rat; 7 in a second curly rat. It will be recalled that our general observation was that gray Norway and curly rats have raucous voices. In contrast, the number of harmonics is from 1 to 3 in mutant albino rats that have clear "musical" voices. The intermediate types in voice quality (black piebald and stub tail) may have more than 3 and less than 6 harmonics in our sample.

Black piebalds tend to have 3 predominant peaks, gray Norway 2, Curlys 1 or 2, stub 1 or 2, but mutant albinos have but one predominant peak. As a result, the mutant albino voice has a whistle quality.

The most constant feature, and one distinguishable to the human ear, is that of the fundamental frequency observed. And it will be remembered that fundamental frequency determines pitch.

All four gray Norway rats tested had a fundamental between 400 and 500 cycles per second, denoting a relatively low pitched voice. All three curlys tested had a fundamental at 500. Three black piebalds had a fundamental at 1000, indicating a medium pitched voice, but one black piebald, also exceptional with respect to number of harmonics, had a voice, the fundamental of which varied between 500 and 800. Five mutant albinos had a high fundamental ranging from 2200 to 2700. There was a suggestion that the fundamental of one of those recorded at 2200 may possibly have been at 1000. These records denoted a very high pitched voice. Of the two stub tail rats for which we have adequate records, one had a fundamental at 1000 and one at 1900, indicating medium high and high pitched voices respectively. Variability in stub rat voices is to be anticipated because the stub tail gene dwarfs the individual animals in various degrees.

Corroborating the auditory impressions of low pitch, we find that gray Norways and curlys have low fundamentals (400-500), black piebalds, with their medium pitched voices, have medium range fundamentals (about 1000), whereas stuf-tail rats and mutant albinos, with their recognized high pitch of voice, may have high range fundamentals (1900-2700). (See figure 1)

Genetic Implications

Because of the inbreeding inherent in the gray Norway strain (King, 1939), it is evident that in general, single-gene-mutant derivative strains will bear much the same residual hereditary background, and hence we may consider most of the idiosyncracies of the mutant derivative strains when compared with the gray Norway source strain as a standard, as being direct effects of the coat-color genes, that mark them.

Upon this reasoning we may say that the curly gene probably tends to lower the voice as does the cinnamon gene. We may suggest that the voice of black animals (not having the gray Norway background) tends to be high in the one case studied. This tendency may be due to the black gene.

When the black gene was combined with the curly gene, we find that a low-pitched voice resulted. It would seem that here the low pitched tendency of the curly with fundamental at 500, dominates in such a combination over the high-pitched voice of the black with fundamental at 2800.

But when Ruby-eye is combined with curly, the fundamental frequency of the voice is raised in the double recessive to 1000.

Stub-tail raises the fundamental frequency to 1000 or more, in our second case, to 1900.

The mutant albino gene raises the fundamental pitch enormously, that is, from the 500 cycle fundamental up to from 2200 to 2700. That this characteristic, clear, whistle voice with very high fundamental, actually segregated together with the albino gene is suggested by the fact that among albinos appearing in later generations from a cross of Wistar albino (purebred for black and piebald) to gray Norway, there were found several animals having the unique, high, clear whistle voice of the mutant albino.

We admit the meagre nature of the direct genetic data, and hope that these suggestions may be checked by future tests upon a significant number of individuals.

DISCUSSION

Voice is a measurable function of structure, and hence our survey suggests that the development of comparable vocal organs together with comparable methods of employment are actually the physical entities determined by the presence or absence of various single genes.

A cursory examination of the vocal organs was undertaken for each of the animals tested. This revealed the curious fact that although there may be some correlation between characteristic strain voice and shape of epiglottis, similar voices within a certain strain may be produced by vocal structures, the epiglottids of which are quite variable in shape.

However, it should not be assumed that the high frequency fundamental component noticed particularly in the case of the mutant

albino rat is necessarily produced by vibration of the vocal cords. Almost all specimens tested exhibited a relatively large component having a frequency between 2000 and 3000 cycles per second. Structural features of mouth and throat cavities may tend to emphasize this frequency. In the case of the high frequency fundamental, it may be produced by the passing of air over an obstruction as in an ordinary whistle, the sound not originating at the vocal cords at all.

It would appear that the fundamental frequency is determined by some sort of vibrating structures such as the vocal cords themselves, the physical nature of which is rigidly determined by the genetics of the individual, and bearing distinct strain variables. This suggests that the vocal cords differ in different strains, at least in length and possibly also in other qualities. Whether or not such physical differences exist histologically, remains to be determined.

It appears also from other evidence, however, that this is probably the case. For example, it is well known that a vibrating wire or fiber emits a tone the fundamental frequency of which is inversely proportional to its length. Suckling mice have tiny, high-pitched voices and short, fine vocal cords. As the cords thicken and elongate during development, the pitch of the voice decreases concomitantly with an increase in raucousness.

A thorough histological study ought to reveal correlations of physical structure with position of the fundamental frequency, and possibly the correlation with more subtile vocal characteristics.

SUMMARY

1. We have recorded and analyzed the voices of rats from eleven distinct strains marked by Mendelian genes.

2. The time qualities of transientness, sustainedness, and varying tone are at present unintelligible because several of these qualities may be found in the voice records of the same individuals. But such variability may be correlated with the nature of the immediate psychological stimulus occasioning the vocal outcry.

3. The number of harmonies seems to increase with increase of auditorily distinguishable harsh quality in the voice.

4. In general, the number of peaks of large amplitude may be said to correlate with quality in that whereas other strains tend to several peaks and have non-whistle quality, the mutant albino voice has but one predominant peak in the animals tested and tends toward a whistle-like voice.

5. Position of the fundamental frequency appears to be the most strain-constant of all the voice qualities, the audibly distinguishable nature of the voices of gray, black piebald, and mutant albino, for example, being corroborated by our wave length analysis.

6. It is noted that quality of voice is hereditary that single coat-color genes can modify it materially. When two modifying genes

may exist in the same individual, the tendency of a characteristic location of the fundamental of one type may actually dominate over the tendency toward another characteristic location.

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XXI

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THE BODY WEIGHT OF COLORPHASE MINK. Clyde E. Keeler and Larry Moore, *Georgia State College for Women, Milledgeville, Georgia.* A population of 1,402 male and 1,295 female, crossbred, ranch mink, all bearing comparable residual hereditary backgrounds, was classified as to simply inherited coat colors. The mean body weight in pounds for each coat color group was compared with the mean body weights for all the other coat color groups. The coat color groups in descending order of mean body weight were: for males 584 Silverblu: 3.32 lbs., 292 Breath of Spring Silverblu: 3.29 lbs., 198 normal dark: 3.15 lbs., 149 Blufrost: 302 lbs., 188 Royal Kohinur: 2.99 lbs. For females they were 511 Silverblu: 2.10 lbs., 273 Breath of Spring Silverblu: 1.99 lbs., 185 normal dark: 1.92 lbs., 133 Blufrost: 1.77 lbs., 193 Royal Kohinur: 1.76 lbs. The mean body weight of Silverblu males, although larger than that of Breath of Spring Silverblu males, is not significantly so. The mean body weight of Blufrost males is larger than that of Royal Kohinur males and the mean body weight of Blufrost females is larger than that of Royal Kohinur females, but in both comparisons the difference is not statistically significant. In the other eight comparisons between male populations, and the other nine comparisons between female populations, the difference between the mean body weights, divided by the standard error of the difference, gives a quotient ranging between 2.7 in one case and 22.7 in another case. Hence these differences are statistically significant. A statistical study was made into the possible influence of litter size, but it was found that litter size has no measureable effect upon adult body size. It was concluded that mutant, colorphase mink tend toward distinct relative sizes in both males and females. It was noted that size differences are indicative of differences in glandular balance which may form an intermediate step between the mutant gene and both temperament and activity modifications observed subjectively to characterize several coat color varieties. Five observers, having handled these varieties over a period of years, agreed that Pastel, Silverblu and Albino are tamer and less active; that Kohinur, Blufrost and Baldy mink are almost if not wholly as active as normal dark mink. Breath of Spring Silverblu, combining the Silverblu and Blufrost characters, is similar to Silverblu in large size, tameness and rate of activity. There is, then, a correlation between both degree of tameness and rate of activity with the possession of a particular body size, which is, in turn, correlated with a distinct mutant coat color.

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CORRELATIONS BETWEEN COAT COLOR, BODY SIZE AND BEHAVIOR IN RANCH BRED MINK.

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INTRODUCTION

At the Ninth International Congress of Genetics held in Stockholm in 1948 evidence was presented for coat color correlations with body size and behavior in ranch bred mink, phenomena related to the general problem of domestication. Silverblu and Pastel genes were shown to possess size increasing tendencies whereas Breath of Spring (Blufrost) and Kohinur (Black Cross) appeared to reduce body size.

During the past decade observations have been continued which confirm the former findings. In addition, several new mutations have arisen that also produce demonstrable effects upon body size. Through cross breeding and genetic segregation

various combinations of these genes permit an examination of gene interaction with respect to body size tendencies.

METHODS

The animals represented in this study were raised on similar diets and with uniform routine care at the Larry Moore Mink Ranch. They were all classified as to coat color and weighed prior to pelting without regard to birth dates which occurred within a few weeks of each other. Upon bringing new color mutations into the herd it was customary to cross the new mutants with the same, highly selected Dark (wild type) strain in order to add vigor. This practice made for uniformity of the residual, hereditary background upon which the mutant genes manifested themselves. All animals of a particular coat color arising from the same type of cross were classified together regardless of other colors segregating in the same litters.

Comparison of coat color groups was made through an examination of their mean size, by computing mean, standard deviation of mean, standard error of mean, difference between means of contrasted populations, and standard error of the difference between the means of contrasted populations. Male groups raised during the same year were compared in the data presented here, unless otherwise stated. Whereas occasionally, a significance of two or more times the standard error of the difference between two means was not obtained, this may be due to small populations or to segregation of unknown factors for size not manifested in the coat color.

RESULTS

Forty-five comparisons show the size increasing tendencies of Silverblu, Pastel and Moyle Buff as well as the slight size reducing tendencies of Ambergold and Palomino. They demonstrate the extreme size reducing tendency of Aleutian. The extremely large size tendency accompanying Moyle Buff is manifest in both homozygotes and heterozygotes. Cameo is neutral.

SILVERBLU COMPARISONS

Dm is difference between means. "Significance" is difference between means divided by the standard error of the difference between the means.

(1) *Silverblu 1955.* 191 Silverblu (carry Ambergold) mean 3.78 ± .0345> 42 Dark (wild type) mean 3.55 ± .0706; dm .23 ± .0785. significance 2.93.

(2) *Silverblu 1956.* 23 Silverblu mean 4.04 ± .1465 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920; dm .51 ± .1729. significance 2.88.

(3) *Silverblu 1956.* 23 Silverblu mean 4.04 ± .1465 > 10 Dark (wild type) mean 3.75 ± .1413; dm .29 ± .2035. significance 1.42.

(4) *Silverblu 1957.* 19 Silverblu mean 4.26 ± .0646 > 27 Dark (wild type) mean 3.94 ± .0967; dm .32 ± .0936. significance 3.43.

Thus, comparisons over a period of three years show Silverblu mink to exceed Dark mink in body weight.

PASTEL

(5) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 42 Dark (wild type) mean 3.55 ± .0706; dm .29 ± .0787. significance 3.68.

(6) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 71 Dark (hybrid for Ambergold) mean 3.46 ± .0659; dm .36 ± .0743. significance 4.84.

(7) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 43 Dark (hybrid for Ambergold and Silverblu) mean 3.68 ± .0745. dm .14 ± .0820. significance 1.71.

(8) *Pastel 1956.* 534 Pastel mean 4.25 ± .0213 > 10 Dark (wild type) mean 3.75 ± .1413; dm .50 ± .1428. significance 3.50.

(9) *Pastel 1956.* 152 Pastel (hybrid for B of S) mean 3.98 ± .0455 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920; dm .45 ± .1020. significance 4.40.

(10) *Pastel 1957.* 222 Pastel mean 4.17 ± .0411 > 27 Dark (wild type) mean 3.94 ± .0967; dm .23 ± .1057. significance 2.17.

From comparisons between Pastel and Dark mink over a period of three years, Pastel is shown to manifest a size increasing tendency, significant in five out of six cases.

BREATH OF SPRING

(11) *Breath of Spring 1956.* 23 B of S mean 4.04 ± .1465 > 19 Silverblu - B of S mean 3.90 ± .1100; dm .14 ± .1832. significance 0.76.

(12) *Breath of Spring 1957.* 222 Pastel mean 4.17 ± .0411 > 13 B of S mean 3.88 ± .1130; dm .23 ± .1057. significance 6 81.

(13) *Breath of Spring hybrids 1956.* 534 Pastel mean 4.25 ± .0213 > 152 Pastel (hybrid for Breath of Spring) mean 3.98 ± .0455; dm .27 ± .0228. significance 11.84.

Breath of Spring are shown to differ very little from Silverblu-Breath of Spring. Breath of Spring are significantly smaller than Pastel. Pastel (hybrid for Breath of Spring) are significantly smaller than Pastel.

AMBERGOLD

(14) *Ambergold 1956.* 23 Silverblu mean 4.04 ± .1465 > 348 Silverblu — Ambergold mean 3.62 ± .0269; dm .42 ± .1489. significance 2.82.

(15) *Ambergold Hybrids 1955.* 42 Dark (wild type) mean 3.55 ± .0706 > 71 Dark (hybrid for Ambergold) mean 3.46 ± .0659; dm .09 ± .0912. significance 0.97.

(16) *Ambergold 1957.* 73 B of S—Aleutian—Silverblu mean 3.79 ± .0591 > 95 B of S—Aleutian—Silverblu—Ambergold mean 3.28 ± .0382; dm .51 ± .0425. significance 12.00.

(17) *Ambergold 1957.* 19 Silverblu mean 4.26 ± .0646 > 377 Silverblu—Ambergold mean 3.76 ± .0253; dm .50 ± .0693. significance 7.21.

(18) *Ambergold 1957.* 47 Silverblu—Aleutian mean 3.72 ± .0824 > 218 Silverblu — Aleutian — Ambergold mean 3.36 ± .0268; dm .36 ± .0866. significance 4.16.

(19) *Ambergold Hybrids 1957.* 136 Ambergold—Aleutian mean 3.75 ± .0358 > 125 Silverblu—Aleutian (hybrid for Ambergold) mean 3.32 ± .0474; dm .43 ± .0585. significance 7.35.

The presence of the Ambergold gene in duplex tends to reduce body weight, and its effect on the heterozygote appears to be marked.

PALOMINO

(20) *Palomino 1957.* 19 Silverblu mean 4.26 ± .0646 > 986 Silverblu-Palomino mean 3.56 ± .0204; dm .70 ± .0325. significance 2.15.

(21) *Palomino Hybrids 1957.* 191 Silverblu mean 3.78 ± .0345 > 154 Silverblu (hybrid for Palomino) mean 3.32 ± .0424; dm .46 ± .0546. significance 8.42.

It would appear that Palomino may express itself in a reduction of size both in homozygotes and heterozygotes.

ALEUTIAN

(22) *Aleutian 1955.* 191 Silverblu (hybrid for Ambergold) mean 3.78 ± .0345 > 13 Silverblu—Aleutian mean 3.35 ± .0468; dm .43 ± .0581. significance 7.40.

(23) *Aleutian 1955.* 42 Dark (wild type) mean 3.55 ± .0766 > 98 Aleutian (hybrid for Silverblu) mean 3.49 ± .0495; dm .14 ± .0866. significance 0.70.

(24) *Aleutian 1955.* 42 Dark (wild type) mean 3.55 ± .0766 > 108 Aleutian (hybrid for Silverblu) mean 3.41 ± .0503; dm .14 ± .0866. significance 1.62.

(25) *Aleutian 1955.* 43 Dark (hybrid for Silverblu and Ambergold) mean 3.68 ± .0745 > 98 Aleutian (hybrid for Silverblu) mean 3.49 ± .0495; dm .19 ± .0894. significance 2.12.

(26) *Aleutian 1955.* 43 Dark (hybrid for Silverblu and Ambergold) mean 3.68 ± .0745 > 108 Aleutian (hybrid for Silverblu) mean 3.41 ± .0503; dm .27 ± .0893. significance 3.02.

(27) *Aleutian 1956.* 10 Dark (wild type) mean 3.75 ± .1413 > 254 Aleutian (hybrid for other genes) mean 3.49 ± .0308; dm .26 ± .1446. significance 1.80.

(28) *Aleutian 1956.* 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920 > 254 Aleutian (hybrid for other genes) mean 3.49 ± .0308; dm .04 ± .0959. significance 0.42.

(29) *Aleutian 1956.* 348 Silverblu—Ambergold mean 3.62 ± .0629 > 73 Silverblu—Ambergold—Aleutian mean 3.37 ± .0491; dm .25 ± .0559. significance 4.47.

(30) *Aleutian 1957.* 236 B of S—Silverblu—Ambergold mean 3.65 ± .0312 > 95 B of S—Silverblu—Ambergold—Aleutian mean 3.28 ± .0382; dm .37 ± .0493. significance 7.90.

Thus, Aleutian produces a reduction in the homozygote weight often of considerable significance.

MOYLE BUFF

(31) *Moyle Buff 1956.* 648 Moyle Buff mean 4.16 ± .0211 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920; dm .63 ± .0938. significance 6.72.

(32) *Moyle Buff 1956.* 648 Moyle Buff mean 4.16 ± .0211 > 10 Dark (wild type) mean 3.75 ± .1413; dm .41 ± .1429. significance 2.87.

(33) *Moyle Buff 1957.* 239 Moyle Buff mean 4.43 ± .0865 > 27 Dark (wild type) mean 3.94 ± .0967; dm .49 ± .1034. significance 4.74.

(34) *Moyle Buff 1957.* 222 Silverblu—Aleutian—Moyle Buff mean 3.88 ± .0294 > 136 Silverblu—Aleutian mean 3.75 ± .0378; dm .13 ± .0463. significance 2.81.

(35) *Moyle Buff 1955 (females).* 99 Silverblu—Moyle Buff mean 2.20 ± .0283 > 196 Silverblu (hybrid for Palomino) mean 2.08 ± .0188; dm .12 ± .0335. significance 3.58.

(36) *Moyle Buff Hybrids 1955.* 333 Dark (wild type, carry Moyle Buff) mean 4.30 ± .0370 > 43 Dark (wild type, carry Ambergold and Silverblu) mean 3.68 ± .0745; dm .62 ± .0745. significance 7.46.

(37) *Moyle Buff Hybrids 1955.* 65 Silverblu (hybrid for Moyle Buff) mean 4.16 ± .0649 > 191 Silverblu (hybrid for Ambergold) mean 3.78 ± .0345; dm .38 ± .0547. significance 6.95.

(39) *Moyle Buff Hybrids 1957.* 52 Dark (hybrid for Moyle Buff) mean 4.32 ± .0739 > 27 Dark (wild type) mean 3.94 ± .0967; dm .38 ± .1217. significance 3.12.

(40) *Moyle Buff Hybrids 1957.* 25 Pastel (hybrid for Moyle

Buff) mean 4.34 ± .0856 > 222 Pastel mean 4.17 ± .0947; dm .17 ± .0949. significance 1.79.

(41) *Moyle Buff Hybrids 1957.* 57 Aleutian (carry Moyle Buff) mean 3.89 ± .0670 > 246 Aleutian (carry Silverblu) mean 3.71 ± .0318; dm .18 ± .0741. significance 2.43.

(42) *Moyle Buff Hybrids 1957.* 217 Silverblu—Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 47 Silverblu—Aleutian mean 3.72 ± .0824; dm .07 ± .0883. signifiance 0.79.

(43) *Moyle Buff Hybrids 1957.* 217 Silverblu—Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 136 Silverblu—Aleutian mean 3.75 ± .0358; dm .04 ± .0475. signifiance 0.84.

(44) *Moyle Buff Hybrids 1957.* 217 Silverblu—Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 125 Silverblu—Aleutian (hybrid for Ambergold) mean 3.32 ± .0474; dm .47 ± .0571. significance 8.23.

(45) *Dark Moyle Buff Allel 1957.* 239 Moyle Buff mean 4.43 ± .0365 > 67 Dark Moyle Buff Allel mean 3.25 ± .0591; dm 1.18 ± .0694. significance 17.00.

DISCUSSION

From the foregoing comparisons it is abundantly evident that Moyle Buff greatly increases body weight in heterozygotes as well as in homozygotes and that the Dark Moyle Buff Allel has no appreciable manifestation in the determination of ultimate body weight.

A number of mink ranchers classify the behavior of mink as *gentle* or *nervous*. Silverblu and Pastel and some of their combinations are thought to be of gentle tendency. Aleutian and its combinations are thought of as tending toward the nervous. (Data are being collected.) Black Eyed White shows tameness tendencies.

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XXIII

THE GEORGIA ACADEMY OF SCIENCE

PIGMENT GENE EFFECTS ON BODILY PROPORTIONS IN MINK

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INTRODUCTION

In studying the constellation of effects associated with single genes in mutant coat-color strains of the long-domesticated Norway rat[1,2] differences in bodily proportion were found between individuals of particular gene constitutions. For example, the bodily proportions of waltzers were altered in that these animals became more stocky[3]. An effect associated with the Hooded gene tended to lengthen the tail[4], and this was evident in several coat color combinations involving the Hooded gene. We interpreted these associated effects to be due to pleiotropic manifestations of single coat color genes, because we could find no rat strains that were free from them.

A preliminary report was presented at the International Congress of Genetics in Stockholm in 1948[5], where two geneticists objected to our interpretation on the grounds that after the coat colors mutated originally other mutations took place in the same chromosome, these subsequent mutations modifying characteristics other than coat color. In this event, the phenomenon would be linkage rather than pleiotropy.

For this reason it would be of interest to examine the recently mutated coat colors of some mammal for similar modifications, since there would be very little opportunity for linked genes to have mutated after the mutation of the coat color genes.

MATERIAL AND METHODS

More than 1,125, skeletal dissections were made on ranch bred mink; the following parts were cleaned and dried for study: from the male the os penis, right tibia, right femur and skull; from the females the right tibia, right femur and skull. The bones were boiled in "Gold Dust" soap powder until the flesh was soft. They were then cleaned, dried and measured with calipers. The cranial capacity was determined by plugging the lesser foramena with wax and then filling the skull through the foramen with magnum fine shot which were then poured into a small graduate cylinder.

Bull. Ga. Acad. Sci. 18: 69-83. 1960.

Most of the mink skeletons studied came from the annual crops and were of approximately the same age. However, a few had been saved as breeders for several years. These latter were examined in order to test the matter of heterogonic growth rates in various parts of the skeleton. For studying bodily proportions each bone measurement of length was recorded relative to the body length of the individual in question. We are studying, then, differences between ratios of statistical populations of bone length divided by body length by comparing their means. If the difference between two means is twice the standard error of that difference, then it is said to be significant (s).

RESULTS

We may compare the bodily proportions of Albinos of an annual crop with Old Albinos saved for several years as breeders. This comparison reveals that as the Albino mink matures more, the relative size of the os penis increases as would be expected. See figure 1. At the same time the tibia, femur and cranial capacity decrease. This simply means that the body length increases at a greater rate than the appendages and cranial capacity, a matter of heterogonic growth.

Albinos		Old Albinos	
		Males	
40 os penis .0732 ± .00032	<	9 os penis .0788 ± .000960	s = 3.5
38 tibia .0951 ± .000354	>	12 tibia .0896 ± .000592	s = 9.0
40 cran. cap. .179 ± .00154	>	12 cran. cap. .168 ± .00273	s = 3.5
		Females	
4 tibia .0967 ± .000785	>	3 tibia .0937 ± .000548	s = 3.1
4 femur .0876 ± .000130	>	3 femur .0855 ± .000499	s = 3.5
4 cran. cap. .166 ± .00238	>	3 cran. cap. .156 ± .00332	s = 2.4

Some data were collected on Screw Neck Pastel females to be compared with Old Screw Neck Pastel.

Screw Neck Pastel		Old Screw Neck Pastel	
		Females	
14 tibia .0941 ± .000527	<	5 tibia .0962 ± .000852	s = 2.1
14 femur .0851 ± .000524	<	5 femur .0861 ± .000232	s = 1.7
14 cran. cap. .166 ± .00220	>	5 cran. cap. .159 ± .00790	s = 0.8

There are also a few data from females of the Pastel-Blufrost combination:

Pastel Blufrost		Old Pastel-Blufrost	
		Females	
13 tibia .0941 ± .000609	<	19 tibia .0947 ± .000404	s = 0.8
14 femur .0847 ± .000495	<	19 femur .0854 ± .000280	s = 1.2
14 cran. cap. .155 ± .00199	>	18 cran. cap. .157 ± .00133	s = 1.6

The relationships here are exactly the same as those found between Screw Neck Pastel and Old Screw Neck Pastel, and in only one item, Screw Neck Pastel tibia, is the difference large enough to be statistically significant.

Normally with greater growth the rates of elongation of tibia and femur decrease relative to the rate of body elongation and the relative rate of cranial capacity increase is reduced. If this is true then in order to prove that we have come upon some alteration of bodily proportions due to presence of a coat color gene, we must demonstrate some violation of these normal heterogonic growth relationships. Otherwise, we have coat-color genes that merely stop development at different points along the normal heterogonic pathway of development.

Thus, if Pastel, for example, that grows larger than Dark mink, should show decrease in tibia length, femur length and cranial capacity, or if Blufrost, that grows less in body length than Dark, should show an increase over dark in tibia, femur, and cranial capacity, divided by body length, we would have to consider those findings merely to be a confirmation of the normal heterogonic growth rates.

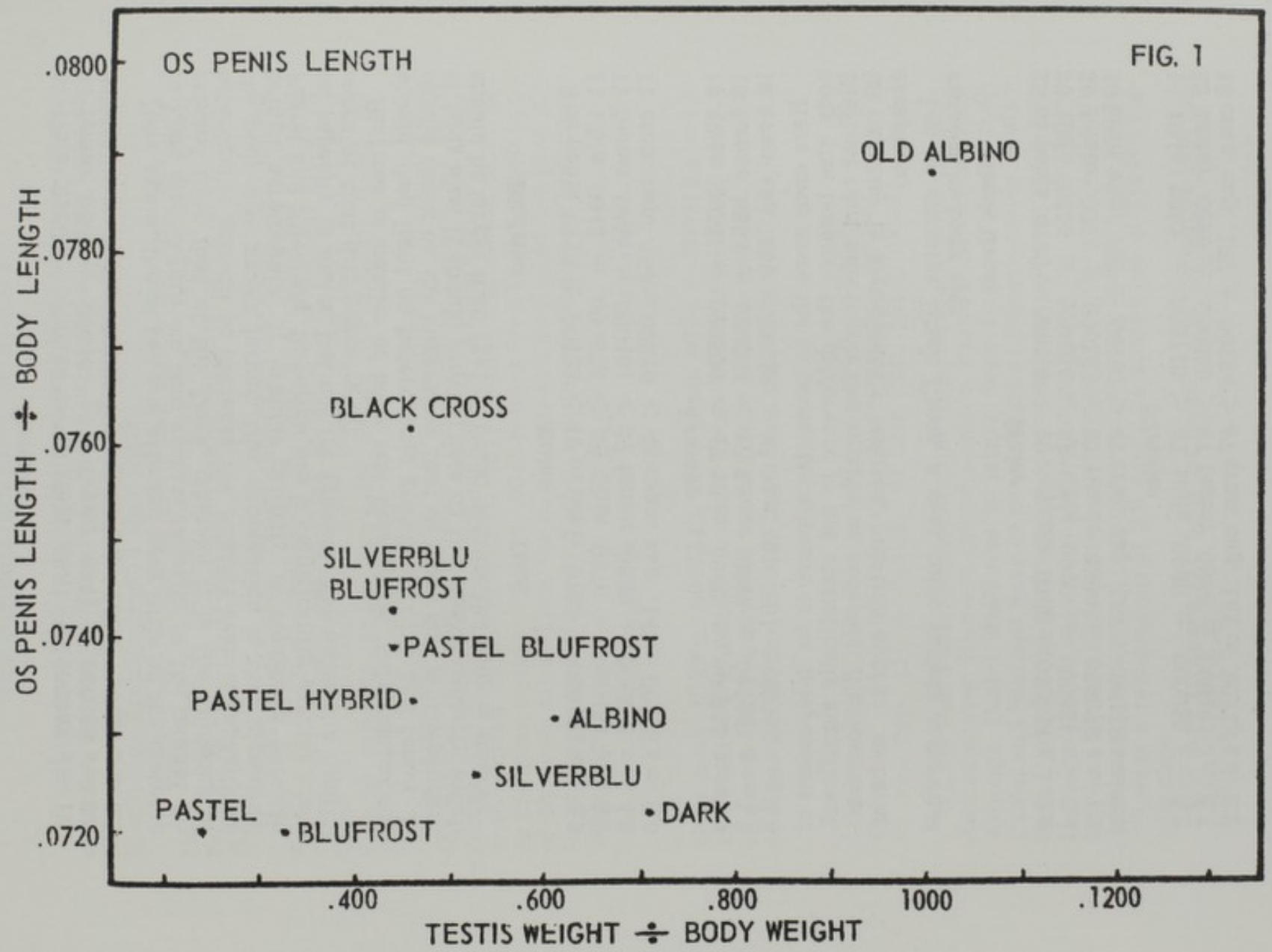
Let us examine Dark in comparison with Pastel, a colorphase type that becomes somewhat larger than Dark in body size.

Dark		Pastel	
		Males	
40 os penis .0723 ± .000511	>	69 os penis .0720 ± .000524	s = 0.4
38 tibia .0970 ± .000451	>	74 tibia .0943 ± .000355	s = 4.7
37 femur .0880 ± .000378	>	75 femur .0854 ± .000540	s = 3.9
41 cran. cap. .163 ± .00118	<	75 cran. cap. .171 ± .00140	s = 4.4
		Females	
47 tibia .0960 ± .000335	>	54 tibia .0935 ± .000899	s = 2.6
47 femur .0863 ± .000461	>	53 femur .0852 ± .000665	s = 1.4
47 cran. cap. .151 ± .00133	<	54 cran. cap. .163 ± .00174	s = 5.5

Thus, we see that tibia and femur relative to body length decreases in Pastels as expected, but curiously enough, cranial capacity increases significantly in both males and females. The os penis does not change to any extent.

Silverblu grows still larger than Pastel, so let us compare Silverblu with Dark.

Dark		Silverblu	
		Males	
40 os penis .0723 ± .00511	<	49 os penis .0726 ± .000403	s = 0.9
38 tibia .0970 ± .000451	>	49 tibia .0956 ± .000403	s = 2.3
37 femur .0880 ± .000378	>	49 femur .0861 ± .000371	s = 3.6
41 cran. cap. .163 ± .00118	<	49 cran. cap. .176 ± .00135	s = 7.3


OS PENIS LENGTH
FIG. 1
OLD ALBINO
BLACK CROSS
SILVERBLU
BLUFROST
PASTEL BLUFROST
PASTEL HYBRID
ALBINO
SILVERBLU
DARK
PASTEL
BLUFROST
.0800
.0780
.0760
.0740
.0720
OS PENIS LENGTH ÷ BODY LENGTH
.400
.600
.800
1000
.1200
TESTIS WEIGHT ÷ BODY WEIGHT

Females

47 tibia .0960 ± .000335 > 36 tibia .0951 ± .000363 s = 1.8
47 femur .0863 ± .000461 > 50 femur .0845 ± .000328 s = 3.2
47 cran. cap. .151 ± .00133 < 50 cran. cap. .162 ± .00121 s = 6.7

Here again, the os penis is affected very little by the increase in body size. Again we find cranial capacity of the mutant increased over that of the Dark, whereas it is the tendency of heterogonic growth to decrease the relative cranial capacity as the body size grows larger. Our explanation is that gigantism brings acromegaly. If cranial capacity is compared between Pastel and Silverblu, Silverblu has a significantly greater cranial capacity in males, but not for females. For males the significance of that difference is 3.7.

Blufrost is smaller of body size than Dark. This comparison should shed light on heterogonic growth of tibia and femur. It should check on the suggestion that os penis size is independent of body size. It should provide data on the cranial capacity which should be larger than that of Dark, because the body is smaller.

Blufrost		Dark	
		Males	
8 os penis .0718 ± .00123	<	40 os penis .0723 ± .000511	s = 0.9
11 tibia .0943 ± .000578	<	38 tibia .0970 ± .000451	s = 3.7
11 femur .0855 ± .000401	<	37 femur .0880 ± .000378	s = 4.5
11 cran. cap. .158 ± .00216	<	41 cran. cap. .163 ± .00118	s = 2.0
		Females	
19 tibia .0957 ± .000566	<	47 tibia .0960 ± .000335	s = 0.4
18 femur .0854 ± .000286	<	47 femur .0863 ± .000461	s = 1.7
19 cran. cap. .156 ± .00121	>	47 cran. cap. .151 ± .00133	s = 2.8

Here once more the os penis size appears to be independent of body size because the difference is not statistically significant. Blufrost tibia and femur are smaller as expected. Blufrost cranial capacity is significantly reduced, but this appears to be an exception.

Let us examine Black Cross, a coat color variety somewhat reduced in body size.

Black Cross		Dark	
		Males	
28 os penis .0700 ± .000706	<	40 os penis .0723 ± .000511	s = 2.6
30 tibia .0955 ± .000454	<	38 tibia .0970 ± .000451	s = 2.4
30 femur .0871 ± .000358	<	37 femur .0880 ± .000378	s = 1.7
30 cran. cap. .168 ± .00167	>	41 cran. cap. .163 ± .00118	s = 2.4
		Females	
15 tibia .0962 ± .000749	>	47 tibia .0960 ± .000335	s = 0.2
32 femur .0869 ± .000655	>	47 femur .0863 ± .000461	s = 0.7
18 cran. cap. .157 ± .00234	>	47 cran. cap. .151 ± .00133	s = 2.2

It will be seen that in everything except Blufrost male-cranial capacity, the comparisons to Dark are as expected on the basis of heterogonic growth. The cranial capacity ratio in Blufrost females is still significantly greater than Dark.

In Black Cross males, os penis and femur are still less than Dark, but cranial capacity is greater than Dark. Black Cross females show tibia, femur and cranial capacity ratios larger than Dark.

It would appear that cranial capacity relative to body length starts out large, as is obvious in most mammals, and that the curve falls off normally in mink at the size of normal Dark. In those color varieties that grow larger than Dark the relative cranial capacity again increases as an acromegalic effect, as shown by Pastel and Silverblu.

The larger growth impetus of Pastel dominates somewhat over the growth retarding influence of Blufrost in crosses. We have recorded one case in which a population of 43 male Pastel-Blufrost with a mean weight of 3.80 ± .0617 pounds was almost as large as the mean weight of 3.82 ± .0345 pounds for a Pastel population of 238 male mink. Thus, we might expect Pastel-Blufrost proportions to approach those of Pastel. Let us compare Pastel-Blufrost with Dark.

Pastel-Blufrost		Dark	
		Male	
40 os penis .0739 ± .000734	>	40 os penis .0723 ± .000511	s = 1.3
40 tibia .0954 ± .00100	<	38 tibia .0970 ± .000451	s = 3.5
40 femur .0871 ± .000956	<	37 femur .0880 ± .000378	s = 0.8
40 cran. cap. .172 ± .000195	>	41 cran. cap. 163 ± .00118	s = 4.0
		Female	
44 tibia .0947 ± .000404	<	47 tibia .0960 ± .000355	s = 2.5
43 femur .0854 ± .000280	<	47 femur .0863 ± .000461	s = 1.7
40 cran. cap. .155 ± .00133	>	47 cran. cap. .151 ± .00133	s = 2.1

We see that Pastel proportions of os penis and cranial capacity dominate over Blufrost proportions in Pastel-Blufrost animals, although Pastel body size is larger than Dark. Whereas both Pastel and Blufrost have os penis lengths proportionately smaller than Dark, Pastel-Blufrost has an os penis proportionately larger than Dark. This may be explained as probably due to interaction between the two mutant coat color genes. The difference is actually 1.8 times the standard error of the difference between the means, whereas a relationship of 2.0 would be considered of proven significance.

We may compare the body proportions of Silverblu-Blufrost with those of Dark.

Males

Silverblu-Blufrost		Dark	
47 os penis .0742 ± .000408	>	40 os penis .0723 ± .000511	s = 2.9
51 tibia .0966 ± .000279	<	38 tibia .0970 ± .000451	s = 1.7
52 femur .0871 ± .000302	<	37 femur .0880 ± .000378	s = 1.9
52 cran. cap. 171 ± .00132	>	41 cran. cap. .163 ± .00118	s = 4.5

Females

8 tibia .0960 ± .000523	—	47 tibia .0960 ± .000335	s = 0.0
8 cran. cap. .162 ± .000264	>	47 cran. cap. .151 ± .00133	s = 3.7

Here we find the same relationship between Silverblu-Blufrost and Dark that we found between Silverblu and Dark. The Silverblu-Blufrost os penis is significantly longer than Dark. Thus, the proportions of Silverblu tend to dominate over Blufrost in os penis length and cranial capacity.

Now that we have compared these homozygotes for two coat color genes with Dark, we should compare the effects of the genes in simplex with each other.

Males

Pastel-Blufrost		Pastel	
40 os penis .0739 ± .000734	>	69 os penis .0720 ± .000524	s = 2.1
40 tibia .0954 ± .000100	>	74 tibia .0943 ± .000355	s = 3.0
40 femur .0871 ± .000956	>	75 femur .0854 ± .000540	s = 1.5
40 cran. cap. .172 ± .00195	>	75 cran. cap. .171 ± .00140	s = 0.0

Females

44 tibia .0947 ± .000404	>	54 tibia .0935 ± .000899	s = 0.0
43 femur .0854 ± .000208	>	53 femur .0852 ± .000665	s = 0.0
40 cran. cap. .155 ± .00133	<	54 cran. cap. .163 ± .000174	s = 3.6

Although three of the comparisons have no significance, it is notable that the Pastel-Blufrost os penis is statistically longer than Pastel and again demonstrates gene interaction. The cranial capacity of Pastel-Blufrost females is less than that of Pastel.

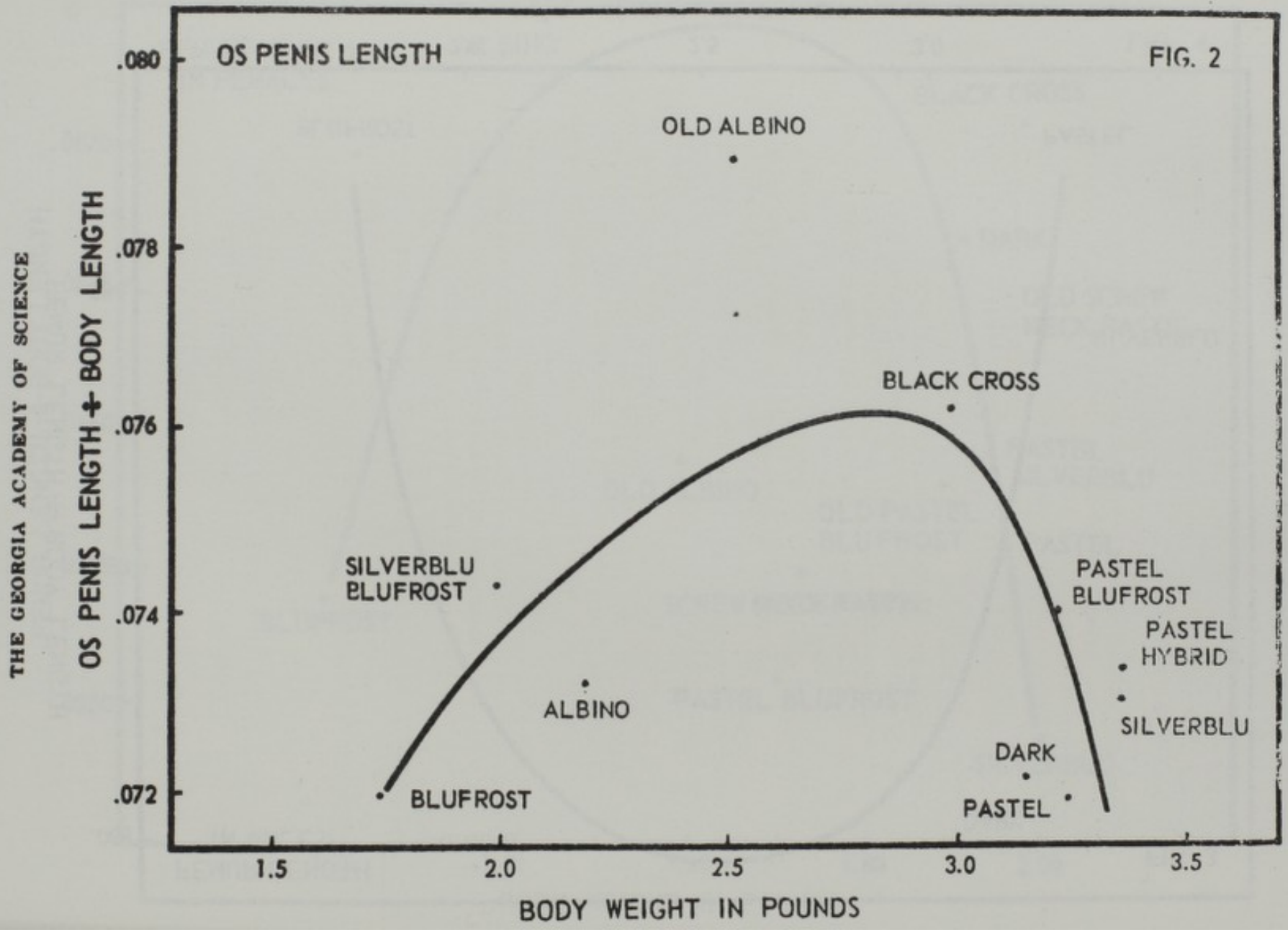
We have some data for comparing Silverblu:

Males

Silverblu-Blufrost		Silverblu	
47 os penis .0742 ± .000408	>	49 os penis .0726 ± .000403	s = 6.3
51 tibia .0966 ± .000279	>	49 tibia .0956 ± .000403	s = 2.0
52 femur .0871 ± .000302	>	49 femur .0861 ± 00371	s = 2.1
52 cran. cap. .171 ± .00132	<	49 cran. cap. .176 ± .00135	s = 2.1

Females

8 tibia .0960 ± .000523	>	36 tibia .0951 ± .000363	s = 1.7
8 cran. cap. .162 ± .00264	—	50 cran. cap. .162 ± .00121	s = 0.0


OS PENIS LENGTH
FIG. 2
OS PENIS LENGTH + BODY LENGTH
.080
.078
.076
.074
.072
OLD ALBINO
BLACK CROSS
SILVERBLU
BLUFROST
PASTEL
BLUFROST
PASTEL
HYBRID
ALBINO
SILVERBLU
DARK
BLUFROST
PASTEL
1.5
2.0
2.5
3.0
3.5
BODY WEIGHT IN POUNDS

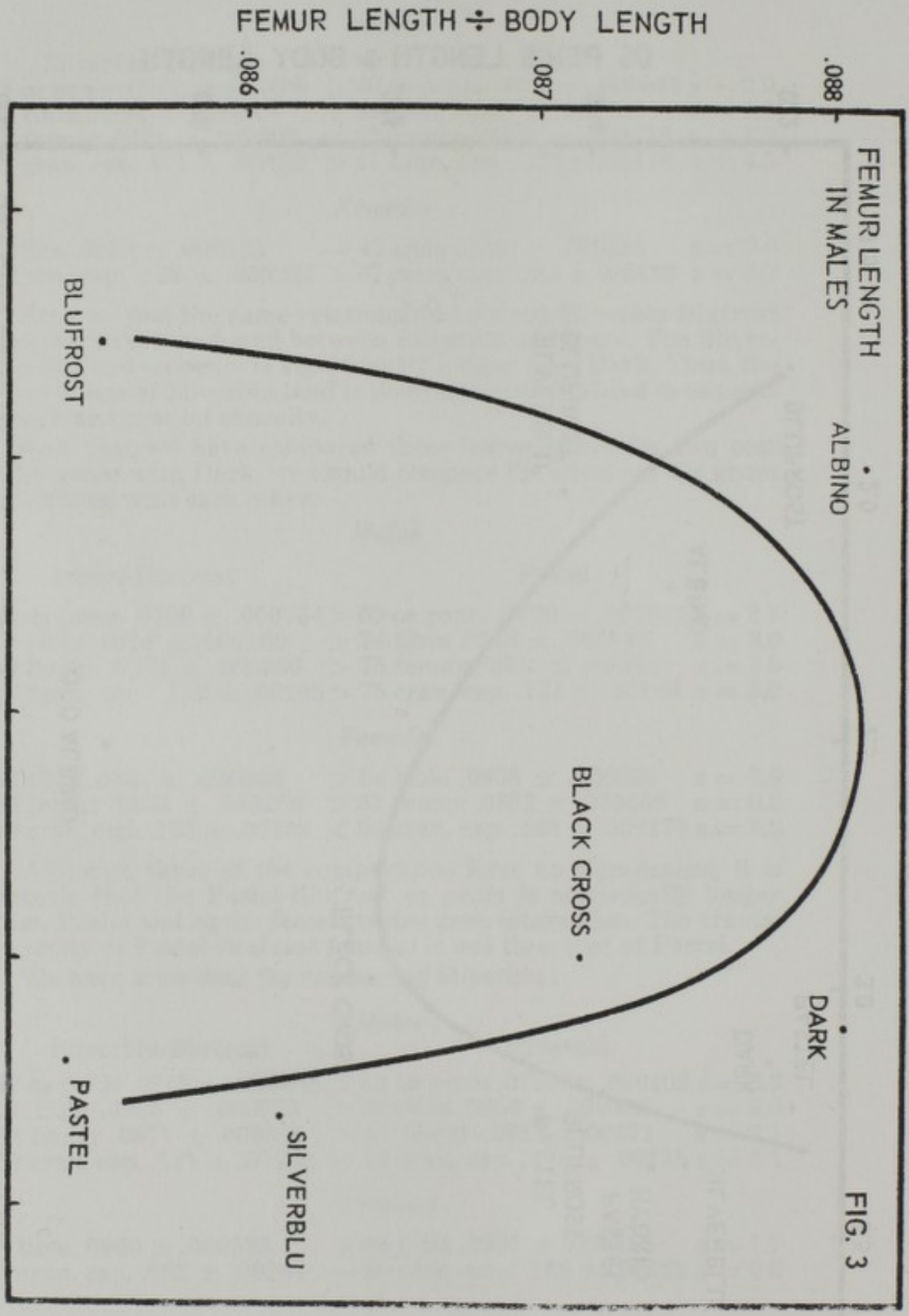
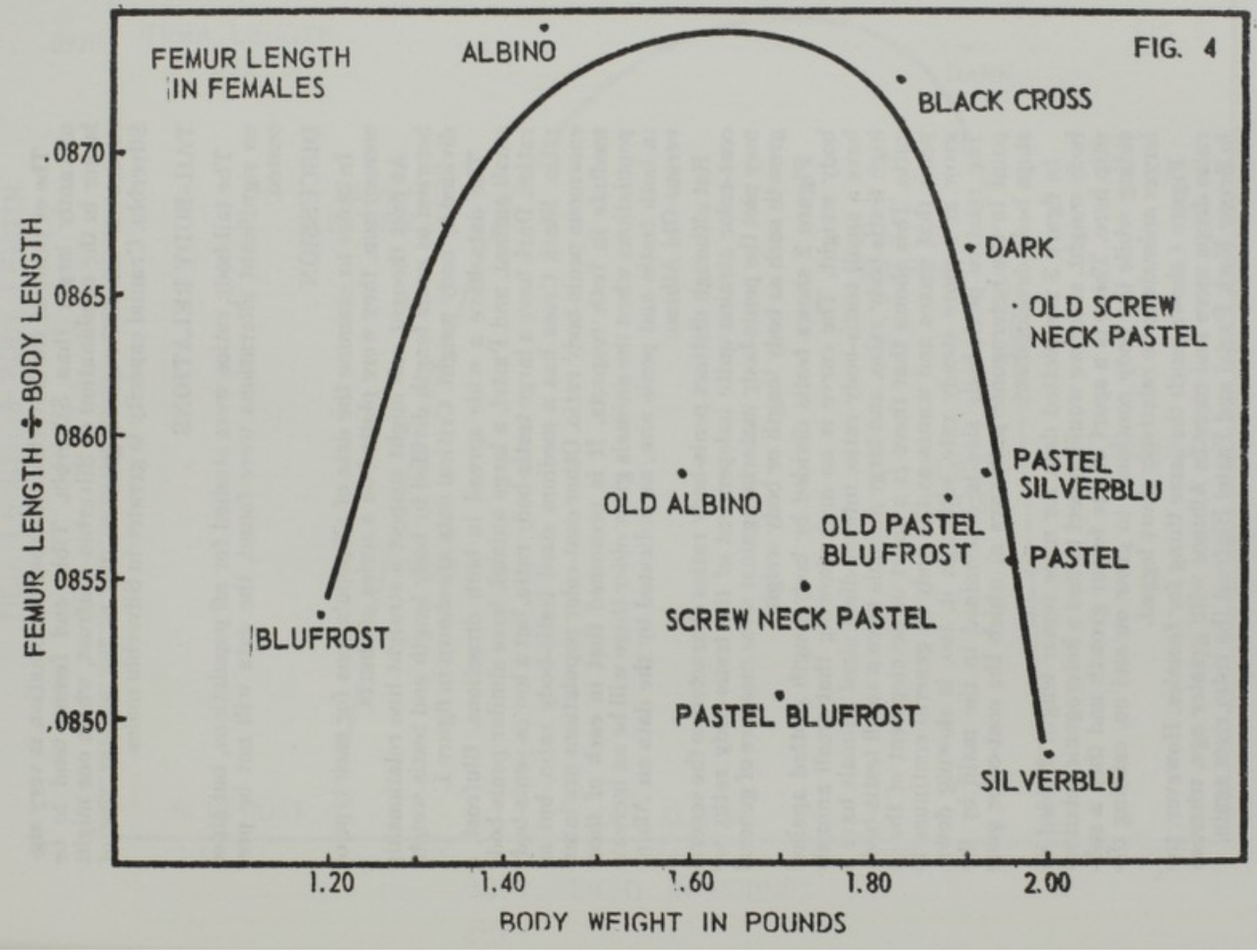

FEMUR LENGTH ÷ BODY LENGTH
.088
.087
.086
FEMUR LENGTH IN MALES
ALBINO
DARK
BLACK CROSS
BLUFROST
SILVERBLU
PASTEL
1.5
2.0
2.5
3.0
3.5
BODY WEIGHT IN POUNDS

FIG. 3


FEMUR LENGTH
IN FEMALES
FIG. 4
ALBINO
BLACK CROSS
DARK
OLD SCREW
NECK PASTEL
PASTEL
SILVERBLU
OLD ALBINO
OLD PASTEL
BLUFROST
PASTEL
SCREW NECK PASTEL
BLUFROST
PASTEL BLUFROST
SILVERBLU
FEMUR LENGTH ÷ BODY LENGTH
.0870
0865
0860
0855
.0850
1.20
1.40
1.60
1.80
2.00
BODY WEIGHT IN POUNDS

The os penis of the Silverblu-Blufrost combination is very significantly larger than Silverblu. Tibia and femur tend to be larger in the combination of Silverblu-Blufrost, which one might expect on the heterogonic grounds due to the greater size of Silverblu. Cranial capacity is greater in Silverblu males.

TAIL-BODY RELATIONS

The tail-body ratios were studied for all populations, but since no significant alterations were found, the data will not be presented.

DISCUSSION

In order to examine the data of all populations for each type of comparison, they were plotted on a series of charts.

At first thought one might suspect a straight line relationship between os penis length divided by body length and testis weight divided by body weight. Critical data are shown in figure 1.

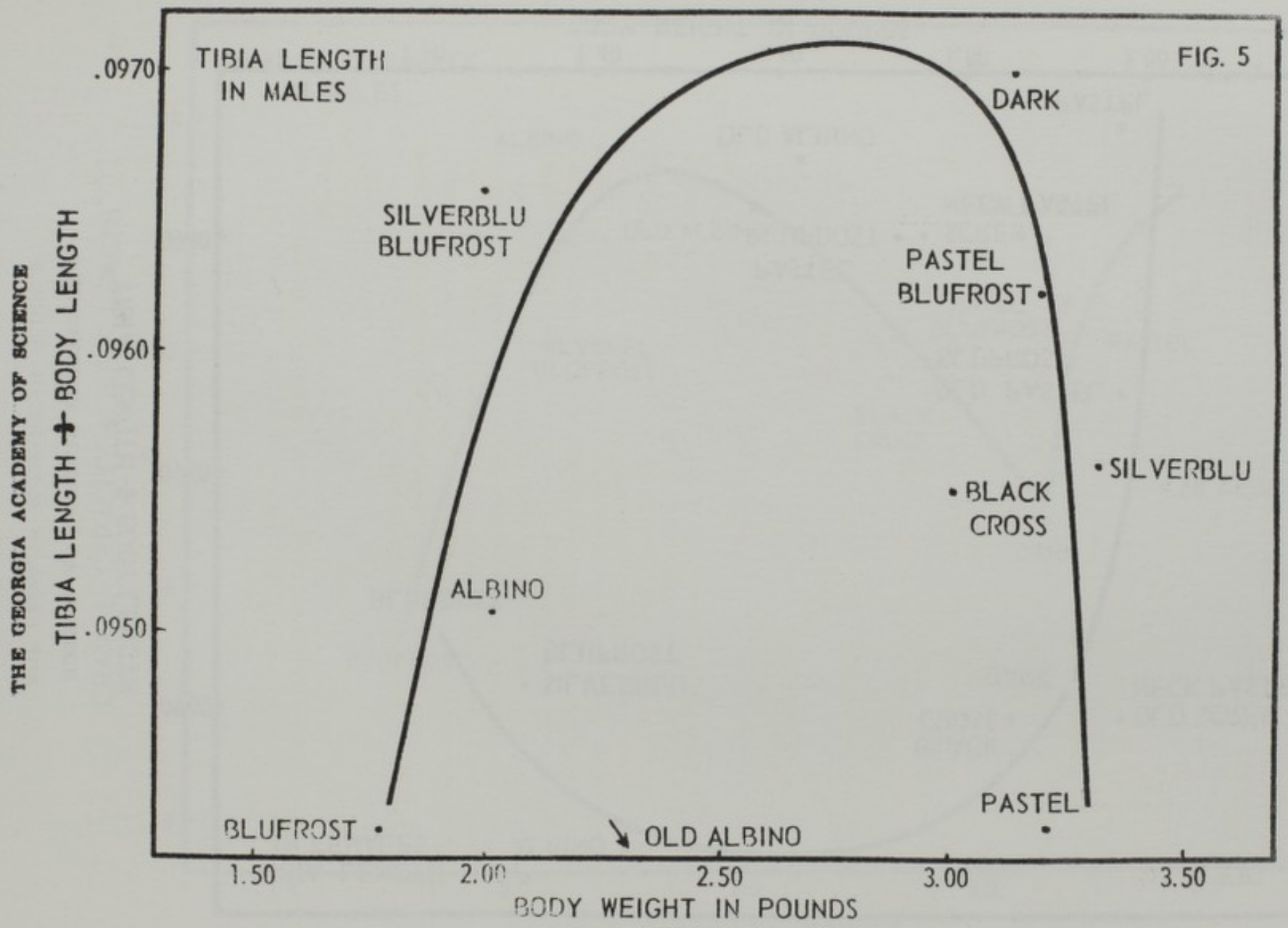
The data have a wide spread in both directions. Blufrost, a small animal, and Pastel, a large animal, have similar penis-body ratios. Dark have a large testis-body ratio, but a low os penis-body ratio. Black Cross has a medium sized testis-body ratio, but an enormous penis-body ratio. Other coat-color populations are intermediate in both respects. It is presumed that in each of these populations when the animals grow older there will be an increase in both testis and penis size, as indicated by the data on Albino versus Old Albino.

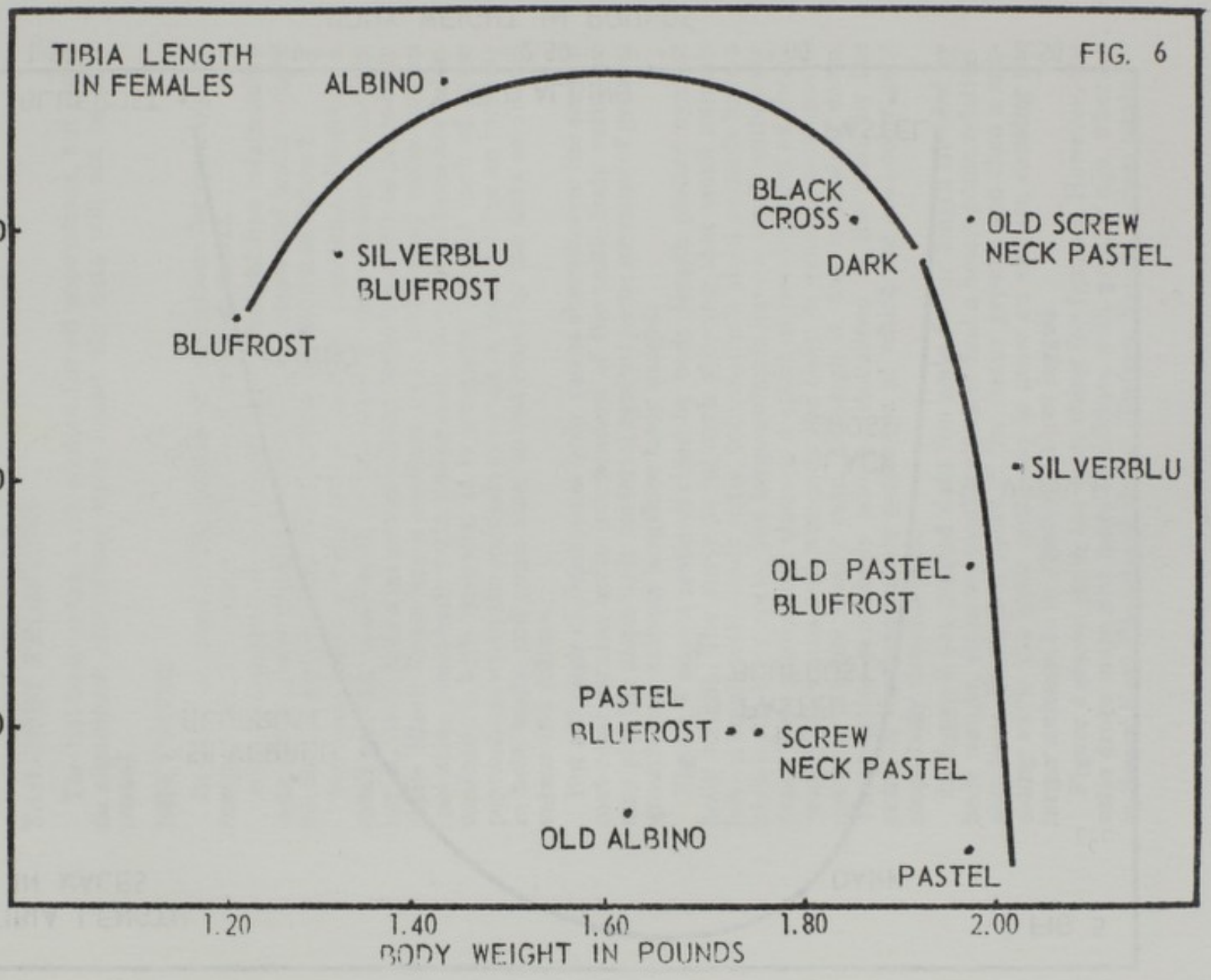
But although distinct penis-body ratios characterize the several coat-color strains quite independent of the testis-body ratio, we may plot the penis-body material against some measure of general growth such as body length or body weight.

Figure 2 shows testis divided by body length plotted against body weight. The curve is an arch showing that small animals have a small testis-body ratio, intermediate sized animals have a high testis-body ratio, and large animals have a small testis-body ratio. This shows that there is a spurt of development of the os penis that waxes and wanes as the body in general continues to grow at a more steady rate, although it, too, is slowing down. The relative penis-body size is determined in the main by the point in the heterogonic pathways at which the coat-color gene stops body development.

In figure 3 are plotted data for male femur length divided by body weight, since we would expect to find a heterogonic relationship here. There is a spurt of the femur growth and then a subsiding while the body continues to grow on and on, causing the larger animals to be relatively short legged.

Figure 4 shows much the same thing for females. However, the ratio drops more and more in Albinos with greater age, whereas in Screw Neck Pastel and Pastel Blufrost the ratio rises again.


TIBIA LENGTH
IN MALES
FIG. 5
.0970
.0960
.0950
TIBIA LENGTH + BODY LENGTH
DARK
SILVERBLU
BLUFROST
PASTEL
BLUFROST
SILVERBLU
BLACK
CROSS
ALBINO
PASTEL
BLUFROST
OLD ALBINO
1.50
2.00
2.50
3.00
3.50
BODY WEIGHT IN POUNDS


TIBIA LENGTH
IN FEMALES
FIG. 6
ALBINO
BLACK
CROSS
OLD SCREW
NECK PASTEL
SILVERBLU
BLUFROST
DARK
BLUFROST
SILVERBLU
OLD PASTEL
BLUFROST
PASTEL
BLUFROST
SCREW
NECK PASTEL
OLD ALBINO
PASTEL
TIBIA LENGTH ÷ BODY LENGTH
.0960
.0950
.0940
1.20
1.40
1.60
1.80
2.00
BODY WEIGHT IN POUNDS

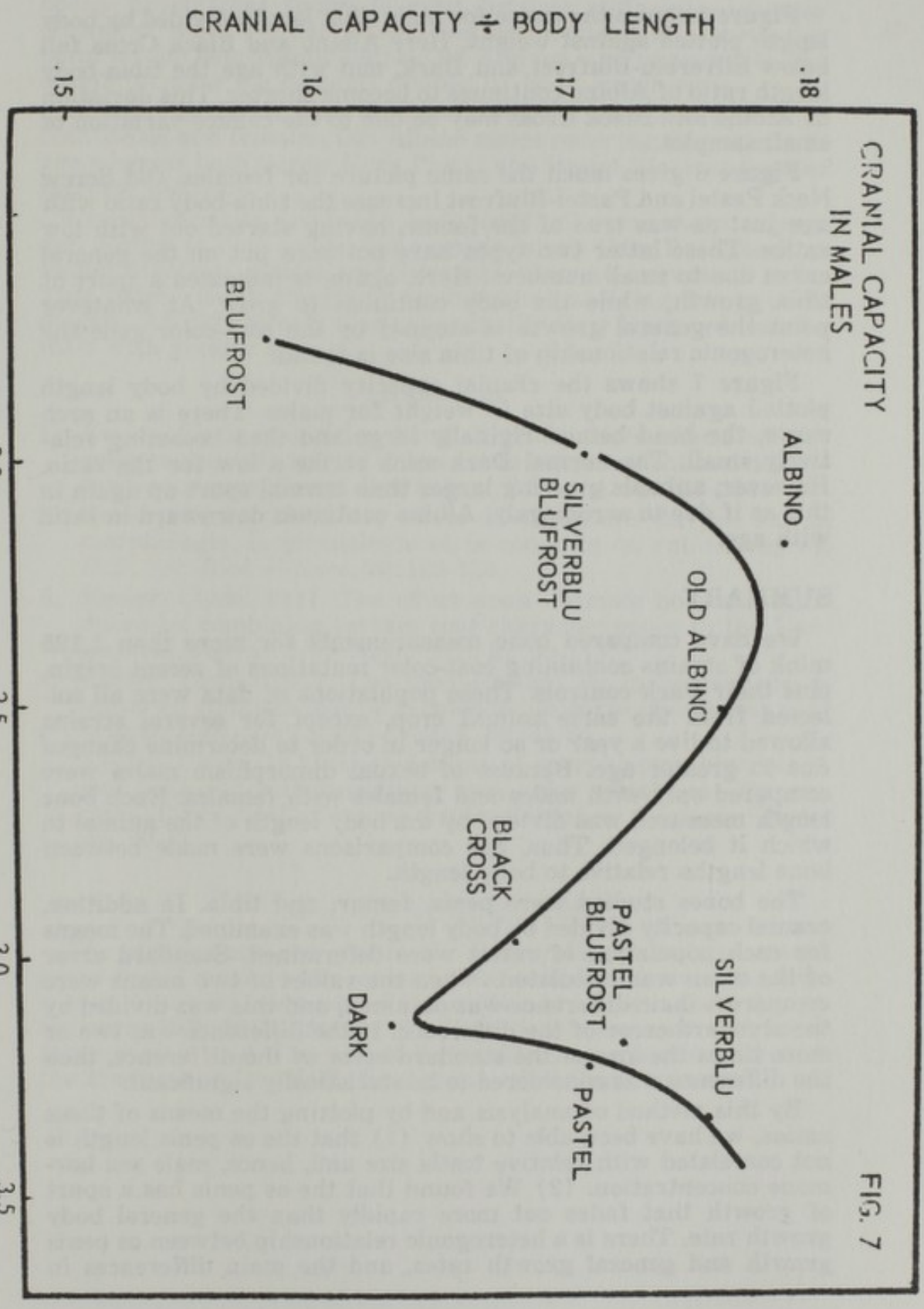

CRANIAL CAPACITY ÷ BODY LENGTH
.15
.16
.17
.18
CRANIAL CAPACITY IN MALES
BLUFROST
SILVERBLU BLUFROST
ALBINO
OLD ALBINO
BLACK CROSS
PASTEL BLUFROST
DARK
SILVERBLU
PASTEL
1.5
2.0
2.5
3.0
3.5
BODY WEIGHT IN POUNDS

FIG. 7

Figure 5 shows the curve for male tibia length divided by body length plotted against weight. Here Albino and Black Cross fall below Silverblu-Blufrost and Dark, and with age the tibia-body length ratio of Albino continues to become shorter. This deviation of Albino and Black Cross may be due to the chance variation of small samples.

Figure 6 gives much the same picture for females. Old Screw Neck Pastel and Pastel-Blufrost increase the tibia-body ratio with age just as was true of the femur, having started out with low ratios. These latter two types have not been put on the general curve due to small numbers. Here, again, is indicated a spurt of tibia growth, while the body continues to grow. At whatever point the general growth is stopped by the coat-color gene the heterogonic relationship of tibia size is found.

Figure 7 shows the cranial capacity divided by body length plotted against body size in weight for males. There is an arch curve, the head being originally large and then becoming relatively small. The normal Dark mink strike a low for the ratio. However, animals growing larger than normal spurt up again in this as if due to acromegaly. Albino continues downward in ratio with age.

SUMMARY

We have compared bone measurements for more than 1,125 mink of strains containing coat-color mutations of recent origin, plus their Dark controls. These populations of data were all collected from the same annual crop, except for several strains allowed to live a year or so longer in order to determine changes due to greater age. Because of sexual dimorphism males were compared only with males and females with females. Each bone length measured was divided by the body length of the animal to which it belonged. Thus, our comparisons were made between bone lengths relative to body length.

The bones studied were penis, femur, and tibia. In addition, cranial capacity divided by body length was examined. The means for each population of ratios were determined. Standard error of the mean was calculated. When the values of two means were compared, their difference was obtained, and this was divided by the standard error of the difference. If the difference was two or more times the size of the standard error of the difference, then the difference was considered to be statistically significant.

By this method of analysis and by plotting the means of these ratios, we have been able to show (1) that the os penis length is not correlated with relative testis size and, hence, male sex hormone concentration. (2) We found that the os penis has a spurt of growth that fades out more rapidly than the general body growth rate. There is a heterogonic relationship between os penis growth and general growth rates, and the main differences in

bodily proportions found to exist between different coat-color strains of mink are due to stopping development at a particular point on the heterogonic paths. Old Albinos, and presumably, the others increase the os penis divided by body length ratio.

Similar spurts of growth were noted for femur and tibia in both males and females, Old Albino males reducing the ratio with age whereas both Screw Neck Pastel and Pastel Blufrost females increase the ratio.

Cranial capacity divided by body length likewise shows a spurt and decline in both sexes, but animals larger than Dark, such as Pastel Bluefrost, Pastel, and Silverblu, show an increase in ratio. This latter rise in the curve we interpret as being due to acromegaly. All old animals of strains smaller than Dark reduced the ratio with greater age.

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XXIV

THE GEORGIA ACADEMY OF SCIENCE

THE DETECTION AND INTERACTION OF BODY SIZE FACTORS AMONG RANCH-BRED MINK

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Introduction

It is well known that when members of large sized races of mammals are crossed with representatives of small sized races, the genetic basis for their differences ordinarily turns out to be dependent upon multiple factors. This was the interpretation given by Castle[2] to his classical, long time study of a cross between English giant and Polish dwarf rabbits. However, if Castle's published material is reexamined,[1,2] one finds a suggestion that all the recessive color mutation classes are actually accompanied by a slightly smaller size than normal. The dominant English spotting pattern is also accompanied by a trend to small body size as compared with its recessive, normal allele. Thus, the color mutations seem to be associated with definite size trends that account for a small amount, but not nearly all, of the multiple-factor differences observed between large and small races. It would appear, then, that a number of other size factors must be involved having no visible correlates in color or other known variations, and for this reason such factors cannot be separated for individual examination.

Presumably, Feldman[4] was the first person to study thoroughly a simple coat color with respect to its associated influences on body size. He found the chocolate pigment variation of the house mouse to be associated with a trend toward larger than average body weight. However, Feldman's paper was not printed until after Green[5], who knew of Feldman's findings, had published conclusive evidence on the same phenomenon associated with chocolate and other genes. Because Castle had not recognized the slight correlations existing between color and size inherent in his rabbit material, Green's findings came as a surprise to him. For this reason Castle and his students, Gates, Reed, and Law, undertook a mouse cross that demonstrated chocolate and other coat color genes to be accompanied by size alteration tendencies, much as Green had described.

At that time it was customary, in interpreting these findings, to believe that the coat color gene was linked with a gene for altered size, rather than that both a color and a size tendency were due to manifestations of the same mutant gene. Castle was for a long time adamant in the then current view.

Various persons, including the present author, then noted (much of the data unpublished) that short-eared mice tend to

Bull. Ga. Acad. Sci. 19: 22-60. 1961.

be small, blue mice tend to be large, wavy mice tend to be small, pink-eyed mice tend to be large, waltzers tend to be small, etc. Some of these trends were so consistent that, because of the wide distribution of mouse stocks, one might suppose that if the mutant gene for a coat color alteration were linked to a gene for body size alteration, cross-overs would have undoubtedly been discovered, and laboratory strains of visible mutants would have been established bearing normal or even opposite trends in size. But this did not happen. The work of Grüneberg[6] on the gray lethal mouse and the findings of others led to a general acceptance of the idea of pleiotropy or multiple manifestations of the same gene allel. However, as late as 1948, many persons at the International Congress of Genetics became skeptical of pleiotropy because of a story that circulated to the effect that a certain highly reputable researcher had proven mathematically that a gene could give rise to one reaction only. Under this restriction, any association between size and color must be due to linkage and not to pleiotropy.

In 1947 the present author[7], upon analyzing the data accumulated by Dr. Henry Donaldson on mutants of the Norway rat, found body length increaser effects associated with chocolate and curly, but body legnth decreaser effects with hooded, albino, ruby eye and waltzer. He showed further[8,9,10] that the decreaser effects associated with ruby eye and hooded tend to cancel the increaser effect of curly in both sexes. Similar effects were detected when body weights of these mutants were compared[11], there being a high correlation between body weight and body length.

The idea was then conceived that because rabbits, rats, and mice represent rodent or rodent-like types, some carnivore newly brought in from the wild should be studied, not only to gather data of greater significance statistically, but also to test the application of these findings to mammals in general. The mutations in such a carnivore group should be followed with regard to size trends over a long period of years from the time the first mutant individual had appeared in order to see if the associated size trends would change.

Combinations of coat colors should be studied carefully to learn (1) if the plus trends are additive and produce very large individuals, (2) if minus trends are additive in the minus direction to produce very small individuals, and (3) if the combination of a plus trend and a minus trend tend to cancel each other out to form average-sized individuals.

It was recognized that certain disadvantages were inherent in the study of carnivores, namely, (1) the high cost of their laboratory production in the great numbers required and (2) the medical care necessary. However, if these animals had a high commercial value, they could be produced in quantity on

ranches, fed a uniform diet, and be cared for through standard procedures, although the research would be limited to examining genetic combinations prepared in anticipation of their marketability.

Ranch-bred foxes were ruled out as experimental animals because of their restricted numbers, although their large size was in their favor.

The ideal animal for these studies has been found to be ranch-bred mink. Mink have been brought in from the wild in fairly recent years and are not yet tame. They are being raised in such great numbers that not a few color phase mutations are cropping out, as might be expected. However, ranches do not ordinarily keep a permanent record of the exact day of birth for each individual mink in the classification register, and birth can take place within a period of about six weeks. This disadvantage is not so bad as it might seem because at pelting time the animals have received almost all of their growth, even though they may be killed within a period of several weeks on very large ranches. Statistically, factors which favor variability are offset to a considerable degree by the large numbers of individuals included in many of the expanded annual populations and their subpopulations of identical genetic background.

Cooperation of the Larry Moore Mink Ranch, located at Suamico, Wisconsin, was obtained, and studies were made on suitable individuals from twelve consecutive annual populations (from 1946 to 1957 inclusive), having a grand total of some 108,717 individuals. This ranch has kept excellent records ever since its founding, and pedigrees have been recorded for all animals.

In order to test whether or not size factors and coat color genes are linked rather than both being pleiotropic manifestations, one should observe the coat colors and sizes over a long period of years. If linked, the size deviation from normal should occasionally separate from the coat color, due to crossing over, but if it is a pleiotropic manifestation of the same gene that produced the coat color, then the same size alteration should forever accompany the color, as mentioned above.

As a development procedure at the Larry Moore Mink Ranch, it was customary to bring in new mutants, in order (1) to cross them to a vigorous, standard Dark strain in order to increase stamina, and then (2) to segregate enough of the new mutants from such a cross to test the value of the new coat color as a market type. The mutants recovered from the cross to standard Dark mink were also (3) combined with other color mutations of proven commercial worth in order to test the color effect of the new mutation in combination with other colorphase types. Thus, the animals included in this study consisted of coat color mutants and combinations of color mutants placed on a relatively

uniform, standard Dark, residual, hereditary background. There were standard Dark mink available with which to compare the study animals.

Because of the variations introduced by commercial production procedures, it would not be supposed that perfect correspondence would be found for all comparisons of the same mutant or combination of mutants. However, one might expect (1) statistical significance in some cases, as well as (2) trends of unproven significance in the same direction.

In the early years of the present study, the investigators dealt mainly with single mutations and their size tendencies as compared with the normal Dark mink strain. However, in the later years many combinations of mutant color genes were produced, giving an opportunity to compare the interactions of various genes with respect to their size effects.

METHOD

Prior to pelting, all animals were classified as to phenotypic appearance and at the time of pelting they were weighed in pounds and tenths of pounds.

Those animals which came from similar matings were recorded in the register in a separate section, together with the individual genetic description and record numbers of their parents in order that pedigrees could be traced. The weight of each individual was recorded. This procedure facilitated selection of new breeding stock each year and provided data from which to gauge the effectiveness of annual selection for larger body size.

This study consisted of collecting into statistical populations the weights of mink of a particular phenotypic constitution. The mean of this color class was determined, together with standard deviation and standard error of the mean. Means of the many combinations produced were compared by routine statistical procedure. Of course, males could only be compared with males, and females with females because of the influence of sex on size. All comparisons had to be made within the same year due to selection for body size and environmental influences, such as variations in food, weather, and slight epidemics. Early and late comparisons are listed in the appendix and are referred to by numbers.

Wherever possible, animals heterozygous for certain recessive coat color genes were not classified together with ones lacking that gene entirely. However, it will be recognized that in segregating populations, heterozygosity for most of the genes studied cannot be distinguished from absence and, as we shall demonstate, significant results may be obtained in many populations in spite of this added factor of variability.

RESULTS

Early Comparisons

In the early years of this study, when Pastel, Breath of Spring, and Silverblu were the most important colorphases on the market, attention was confined mainly to comparing the sizes of animals of these colors with Dark mink. A series of these comparisons is given in the appendix under the title, Early Comparisons.

Without going into detail about all of these, we find that Silverblu tends to be larger than Dark in males:

Appendix No.	*year*	*dm**	*s*	*increase*
(1)	1946	.17	4.0	5.1%

Silverblu females are also larger than Dark females:

Appendix No.	*year*	*dm*	*s*	*increase*
(9)	1946	.18	11.2	8.6%

Breath of Spring males are smaller than normal Dark:

Appendix No.	*year*	*dm*	*s*	*decrease*
(18)	1946	.13	2.5	4.2%

This is also true for Breath of Spring vs. Dark comparisons for females.

Appendix No.	*year*	*dm*	*s*	*decrease*
(22)	1946	.15	6.5	7.8%

In 1946 the increase in size of Silverblu was compared with the decrease in size accompanying Breath of Spring. In both males and females, these opposite effects tended to cancel each other.

In 1946 Silverblu males were larger than Dark by 5.1%, but Breath of Spring-Silverblu males were 4.3% larger, as shown in in comparison in the Appendix No. (25).

In 1946 Silverblu females were larger than Dark by 8.6%, but Breath of Spring-Silverblu females were 3.5% larger than Dark, as shown in the comparison in the Appendix No. (31).

Black Cross was a white-spotting gene mutation that proved not so popular as some of the other colorphase types, and hence was discontinued after several years. However, during the time that it was under observation, it was definitely proven to be due to a size reducer gene.

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* dm is difference between means. s is significance which represents the difference between means divided by the standard error of the difference between means.

Appendix No.	*year*	*dm*	*s*	*decrease*
males (37)	1946	.16	4.2	5.1%
males (38)	1947	.22	3.05	6.4%
females (39)	1946	.16	7.3	8.9%
females (40)	1947	.15	4.54	7.2%

Much the same story is told by data collected during the next six years, so details of this period are not included here. Discussion of data resumes with those for the annual crop of 1954. By this time several new colorphase genes had been crossed to standard Dark and then extracted again in F2. In addition, numerous combinations were available for a study of the interactions between the size effects of colorphase genes.

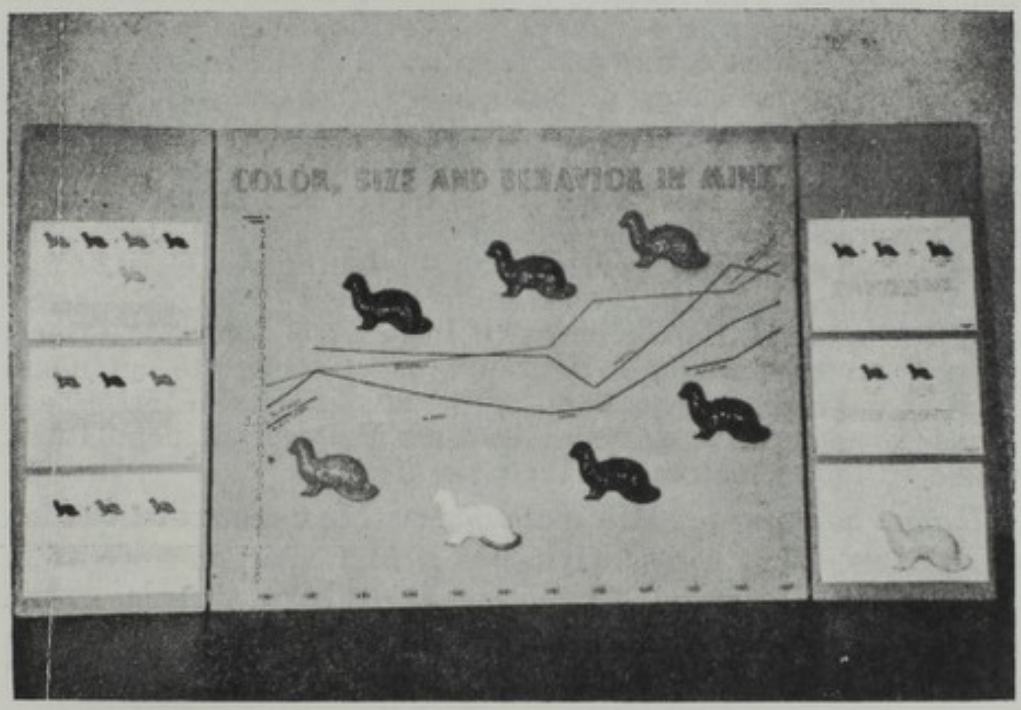


CHART 1. *Chart exhibited at International Congress of Genetics, Montreal, 1958, showing the effectiveness of general selection of unidentified multiple factors for body size in this population for the twelve year period studied. The points on the chart represent actual mean weights of annual populations in pounds and tenths of pounds for the years indicated. On the side wings are shown certain cases of gene interaction affecting body size.*

Later Comparisons

Although about twenty mutations were processed during the time of this study, most of them were soon eliminated as not having market possibilities. Of those remaining, the most important were Silverblu, Pastel, Aleutian, Breath of Spring (Blufrost), Ambergold, Palomino, and Moyle Buff. A small amount

of data was available on Albino which represents really a pigment level in the albino series corresponding to Siamese of the cat and Himalayan of the rabbit. It is of academic interest because in addition to pink eyes, it possesses sooty nose, ears, feet, and tail. When compared to black-eyed white, it is seen to have a small amount of yellow in the body coat.

During the twelve years covered by these observations, selection for larger size was practiced in choosing breeders to produce the annual expanded populations. Consequently, as shown in Chart No. 1, the body size increased rather constantly with chance fluctuations, as might be expected. Unfortunately, the greatest deviation from this gradual increase in size was in the normal Dark control strain where one serious mistake in selection was made. This resulted from finding in the breeding stock a male of such superb vigor, conformation, and fur qualities that it was assumed that his "smaller than the best" size was due to having been born a runt and then having suffered from the natural competition with his litter mates. Unfortunately, after he had been bred into most of the normal Dark stock, his "smaller than the best" size turned out to be genetic, and this fact lowered the average body size of the control stock. The situation was gradually remedied by eliminating the blood of this individual animal from the breeding list and by rigorous selection. Fortunately, the deviation of the control stock for several years from what would be desired was not enough to invalidate most of the comparisons, and had the normal Dark control been rendered useless, comparisons between the mutant populations would still have maintained their significance.

It may be argued that a mutant gene produces a distribution of variates about a mean lying at a particular distance from the mean of the normal distribution. For this reason some of the sample populations bearing this gene will lie so close to the normal mean that the distance to the mutant means will be of unproven statistical significance. It follows that in calculating the approximate position of the mutant mean relative to the position of the normal mean, one should include the mutant populations so close to the normal mean as to be of unproven statistical difference, as well as those of proven statistical difference from the mean of the normal population. Otherwise, if one includes only those populations of statistically proven distance, one will arrive at a collective estimate of the position of the mutant mean farther away from the normal mean than it actually is. Hence in the charts of this study, except for questionable populations of very few variates or of extremely low significance, all populations have been included.

Silverblu

Silverblu animals tend to be larger than normal Dark. There are five male comparisons that illustrate this point.

Appendix No.	*year*	*dm*	*s*	*increase*
(3)	1954	.02	—	0.52%
(4)	1955	.23	2.93	4.68%
(5)	1956	.51	2.88	14.45%
(6)	1956	.29	1.42	7.73%
(7)	1957	.32	3.43	8.12%

In the tables, as in the appendix, dm = difference between means (in pounds) of the two populations compared, and s = significance or difference between means divided by the standard error of the difference between the two means.

The 1954 data, although tending in the same direction as the other comparisons, show very little difference between means. It may be even questionable to include this item because of possible interaction between Silverblu and Moyle Buff involved in the comparison, so it will be omitted from consideration.

Of importance, however, is the fact that the average increase in size of Silverblu is 8.74% above normal Dark, taken in each case as 100%.

Silverblu female comparisons are as follows:

Appendix No.	*year*	*dm*	*s*	*increase*
(15)	1954	.13	2.56	6.53%
(16)	1955	.24	6.78	12.56%
(18)	1955	.13	4.26	7.80%

The Silverblu females exceed the Dark females by an amount quite similar percentage wise, to the males. The average percentage increase is 8.96.

As will be seen later on, Aleutian tends to be smaller than Dark and hence it is not surprising to find in comparison (Appendix, No. 1) that Silverblu Males are significantly larger than Aleutians. In fact, Silverblu males are 5.77% larger than Aleutians in this case.

Appendix No.	*year*	*dm*	*s*	*increase*
(11)	1954	.12	2.15	5.77%
(12)	1954	.04	1.96	——
(19)	1955	.16	1.56	7.80%
(21)	1956	.03	1.39	1.50%

Female comparisons are not so satisfactory as male comparisons. Comparisons No. (11) and (19) show about 6.78% difference. Comparison No. (11) is statistically significant, but Nos.

(19) and (21), though in the right direction, still lack statistical significance. Comparison No. (12) is in the wrong direction and lacks statistical significance.

There is one comparison, No. (2), which tests the effect of Silverblu on Breath of Spring-Aleutian. For this comparison dm is only .06. The populations compared consisted of 422 Silverblu-Breath of Spring-Aleutians and 115 Breath of Spring-Aleutians, but the s is 1.57 and hence not of proven significance.

There are two female comparisons, Nos. (14) and (20), testing the effect of Silverblu on Breath of Spring-Aleutian. For comparison No. (14) the Breath of Spring-Aleutian population has a mean actually larger than the Silverblu-Breath of Spring-Aleutian, but the difference is of practically no significance.

However, for comparison No. (20) the Silverblu-Breath of Spring-Aleutians exceed the Breath of Spring-Aleutians with a dm of .11 and a significance of 2.92. The difference actually represents about 5.53%.

Silverblu was compared with Pastel in No. (8) and in No. (13). In the first comparison Silverblu exceeded Pastel by .12 pounds, with a significance of 2.10. In the other case the dm was only .04, and this difference had practically no significance.

There is one comparison of Silverblu-Ambergold females with Dark, No. (17). In this case the dm is .11 pounds, and the significance is 3.66.

The interaction between Silverblu and Aleutian in males is tested in (9), but the result did not differ from Silverblu in this comparison.

Two comparisons that show the reducing effect of Aleutian upon Silverblu are Nos. (36) and (37).

Appendix No.	*year*	*dm*	*s*	*decrease*
(36)	1954	.16	2.88	7.27%
(37)	1954	.08	1.79	3.77%

Comparison No. (36) shows a significant reduction and No. (37) a lesser reduction, but even this approaches significance. The average percentage difference is 5.52.

The interaction between Breath of Spring and Silverblu was tested in No. (10). The dm is .08 and the significance is 1.1, suggesting a reducing tendency of Breath of Spring.

When Silverblu is combined with Moyle Buff, No. (22), the combination was larger than Moyle Buff alone. The dm was .06 and the s of 1.76 approached significance.

Thus, for Silverblu a tendency to greater size than Dark in both males and females may be confirmed, and an increase of about 5.52%. Silverblu is definitely larger than Aleutian in No. (11) and possibly in Nos. (19) and (21). The increase overcomes Aleutian decrease in No. (1). Silverblu increase is can-

celled completely in No. (14) and partially in Nos. (2) and (10). Only in No. (20) is Silverblu able to significantly overcome the reducing combination of Breath of Spring and Aleutian in females. In No. (22) there appeared to be a tendency for the increaser effects of Silverblu and Moyle Buff females to be additive. Silverblu was significantly larger than Pastel among females in one case, No. (8).

Aleutian

More comparisons are available for Aleutian males than for Silverblu males. Comparisons of Aleutian with Dark are as follows:

Appendix No.	*year*	*dm*	*s*	*decrease*
(28)	1955	.14	.07	3.94%
(29)	1955	.14	1.62	3.94%
(30)	1955	.19	2.12	2.12%
(31)	1955	.27	3.02	7.34%
(32)	1956	.26	1.80	6.93%
(33)	1956	.04	0.42	1.13%

In each case Aleutian males are smaller than Dark males. The comparison, No. (33), may not be quite justified because of the miscellaneous nature of the Dark group. Several of the comparisons, Nos. (30) and (31), are definitely significant, and two others, Nos. (29) and (32), approach significance. The average percent of reduction is 4.23.

There are two comparisons of Aleutian females with Dark females.

Appendix No.	*year*	*dm*	*s*	*decrease*
(38)	1954	.09	2.83	4.52%
(40)	1955	.08	1.89	3.76%

One of these comparisons, No. (38), shows Aleutians to be significantly smaller than their controls. The other, No. (40), shows a reduction in the Aleutians approaching the point of twice the standard error of the difference, actually 1.89. Their average percentage reduction is 4.14.

The effect of Aleutian on the Silverblu-Ambergold combination is definite. Male comparisons are as follows:

Appendix No.	*year*	*dm*	*s*	*decrease*
(34)	1956	.25	4.47	7.42%
(35)	1957	.37	7.90	10.14%

The average percentage reduction is 8.78.

Aleutian cancels the increase effect of Silverblu in two out of three comparisons.

Appendix No.	*year*	*dm*	*s*	*decrease*
(25)	1954	.18	3.61	5.20%
(26)	1954	.07	1.00	2.09%
(27)	1955	.43	7.40	12.83%

The average reduction of the two having significance is 9.01%.

Among females comparison No. (43) was obtained between Aleutian-Silverblu and Ambergold-Silverblu. Aleutian-Silverblu are larger. The dm is .10, the significance is 4.85. This may mean that Silverblu has more effect in combination with Aleutian than with Ambergold. However, comparison No. (41) shows that Aleutian added to Silverblu-Breath of Spring may produce animals of about the same size as when Ambergold is added to Silverblu-Breath of Spring. The dm is .01, the significance 0.15.

Aleutian definitely reduces the Breath of Spring-Silverblu combination.

Appendix No.	*year*	*dm*	*s*	*decrease*
(23)	1954	.24	3.5	7.45%

Aleutian has a greater reducing effect upon the Breath of Spring-Silverblu combination than has Palomino.

Appendix No.	*year*	*dm*	*s*	*decrease*
(24)	1954	.14	3.6	4.55%

When Aleutian is added to Moyle Buff in females, it significantly reduces size, according to comparison No. (42). The dm is .12, the significance is 2.64, and the body size reduction is 5.58%.

There is a comparison, No. (39), in which Silverblu females hybrid for Aleutian are found to be larger than Silverblu hybrid for Ambergold. The dm is .08, and the significance is 1.16. This is suggestive but not to be taken too seriously.

Pastel

There are a number of comparisons of Pastel (chocolate) males with Dark males and several for females.

Appendix No.	*year*	*dm*	*s*	*increase*
		Males		
(46)	1955	.29	3.68	8.17%
(47)	1955	.36	4.84	10.41%
(48)	1955	.14	1.71	3.80%
(49)	1956	.50	3.50	13.33%
(50)	1956	.45	4.40	12.75%
(51)	1957	.23	2.17	5.84%
		Females		
(52)	1954	.09	2.75	4.52%
(53)	1956	.12	6.31	5.55%

Of these eight comparisons all but No. (48) are of significance, and No. (48) approaches significance, showing the size increasing tendency of the Pastel gene. The average percentage increase for males is 9.05, and for females is 5.03.

There are two comparisons of Pastel females with Dark.

Appendix No.	*year*	*dm*	*s*	*increase*
(52)	1954	.09	2.75	4.52%
(53)	1956	.12	6.31	5.55%

Thus, Pastel females are also significantly larger than Dark females. The average increase is 5.03%.

Pastel may be manifested to a certain extent in hybrids as indicated by comparison No. (55). The dm is .15, the significance is 3.02, and the increase is 6.94%.

When Pastel, combined with Breath of Spring, is compared with Aleutian combined with Breath of Spring, the former are significantly larger, as shown in No. (54), in which the dm is .15, the significance is 3.06, and the percentage difference is 6.84.

There is a comparison, No. (45), of the effect of Pastel on Breath of Spring. The dm is .24 and the significance is 4.21. However, the direction is wrong, possibly meaning that the Pastel-Breath of Spring is a relatively weak combination.

When Pastel-Breath of Spring males were compared with Silverblu-Breath of Spring, Pastel developing males exceeded those containing Silverblu by a dm of .12 and a significance of 1.51.

Breath of Spring

The reducing effect of Breath of Spring may be demonstrated by many comparisons. When Breath of Spring males were compared with Pastel, No. (64), the former were found to be smaller by a dm of .23 and a significance of 6.81.

There are two comparisons showing the effect of Breath of Spring on Pastel.

Appendix No.	*year*	*dm*	*s*	*decrease*
(59)	1954	.21	3.1	5.86%
(60)	1955	.02	0.28	0.52%

Comparison No. (59) shows a significant reduction because of Breath of Spring, but No. (60) is of no value, possibly because of the few animals, 48 in number, composing the Breath of Spring-Pastel population.

When combined with Aleutian, Breath of Spring may tend to decrease the size still further, according to No. (56). The dm is .05, and the significance is not proven, being 1.1.

Among 1954 females, comparison No. (67), Breath of Spring added to Aleutian reduced the mean .06 pounds below the Aleu-

tian mean. The significance is 1.99 and hence almost satisfactory. The decrease is 2.88%.

A similar test on 1955 females, comparison No. (68), gave a dm of .06 and a significance of 1.61, which approaches the 2.00 point considered as satisfactory.

A test of the effect of Breath of Spring on Pastel in 1955 gave a dm of .06 and an almost satisfactory significance of 1.87.

A second test on 1956 females was not satisfactory, as shown in comparison No. (72). The dm is .01, and the significance only 0.30.

Among 1954 females, comparison No. (66), there was revealed no significant reduction of Pastel by adding Breath of Spring. However, in two of the three cases just described, the Breath of Spring Pastel is smaller than the Pastel. When combined with Silverblu, comparison No. (58), it reduces size significantly. The dm is .11, the significance is 2.14. There is one comparison, No. (62), in which populations of only 23 and 19 animals were used, and the comparisons cannot be trusted. There was no significant difference between the means, and the Breath of Spring-Silverblus were actually a trifle larger than the Breath of Spring.

There are two male comparisons, Nos. (57) and (61), in which the effect of adding Breath of Spring to Silverblu-Aleutian is tested.

Appendix No.	*year*	*dm*	*s*	*decrease*
(57)	1954	.06	2.00	1.83%
(61)	1955	.05	0.72	1.41%

In No. (57) Breath of Spring significantly reduces the size of Silverblu-Aleutian, and in No. (61) the *dm* is similar, but there are not sufficient animals in the populations compared to provide statistical significance. (The Silverblu-Aleutian population contained only 13 animals.)

There are three comparisons testing the effect in females of Breath of Spring on the Silverblu-Aleutian combination.

Appendix No.	*year*	*dm*	*s*	*decrease*
(65)	1954	.03	1.55	1.47%
(69)	1955	.11	3.47	4.98%
(73)	1956	.10	2.67	5.00%

In two cases the presence of Breath of Spring reduces size with satisfactory significance. The average percentage reduction is 3.81.

Ambergold

Satisfactory Dark controls with which to compare Ambergold are not available. However, its effects on other gene mutations

and certain combinations of mutations can be determined.

In comparison No. (75) it seems possible, but not proven, that Ambergold reduces size when present in the hybrid. The reduction is .09, but the significance is only 0.97.

The reducing effect of homozygous Ambergold on Silverblu may be demonstrated by the following comparisons.

Appendix No.	*year*	*dm*	*s*	*decrease*
(74)	1956	.42	2.82	10.40%
(77)	1957	.50	7.21	11.74%

It will be noted that these reductions are quite significant.

There is another comparison of interest in this connection, namely No. (81). Ambergold-Silverblu is compared with Silverblu-hybrid for Ambergold. The hybridity for Ambergold seems to have reduced the body size of Silverblu (as suggested above), so that no significant difference between this and Ambergold-Silverblu is observed.

Comparison No. (80) shows that Ambergold has a greater reducing effect on Silverblu than that produced by Aleutian. The dm is .08, the significance is 2.68.

Adding Ambergold to the Breath of Spring-Silverblu-Aleutian combination produces a reduction in size.

Appendix No.	*year*	*dm*	*s*	*reduction*
(76)	1957	.51	12.00	13.46%
(78)	1957	.36	4.16	9.68%

The reduction made by Ambergold in hybrid males can be demonstrated by a 1957 comparison not listed in the appendix in which 47 Silverblu-Aleutian mean $3.72 \pm .0824 > 125$ Silverblu-Aleutian (hybrid for Ambergold) mean $3.32 \pm .0474$. dm = .40. s = 4.21. Reduction = 10.72%.

The reduction tendency of hybrid Ambergold seems also to be involved in comparison No. (79). In this case Ambergold-Aleutian is larger than Silverblu-Aleutian when hybrid for Ambergold. The dm is .43, the significance is 7.35, and the percentage reduction is 12.95%.

Palomino

Palomino in males definitely reduces Silverblu as shown by comparison No. (83). The dm is .70, the significance is 2.15, and the percentage reduction is 16.44%.

Palomino in males also reduces Breath of Spring-Silverblu, as shown in No. (82). The dm is .38, the significance is 5.19, the percentage reduction is 10.98%.

Palomino has an effect on hybrids, as shown by comparison No. (84). The dm is .46, the significance is 8.42, and the percentage reduction is 12.17%.

Moyle Buff

Moyle Buff carries with it such a strong tendency to large size that six comparisons of males and three out of four comparisons among females are significant.

There are three comparisons of Moyle Buff males with Dark.

Appendix No.	*year*	*dm*	*s*	*increase*
(87)	1956	.63	6.72	17.85%
(88)	1956	.41	2.87	10.93%
(89)	1957	.49	4.74	12.44%

Two female comparisons show Moyle Buff to be significantly larger than Dark mink.

Appendix No.	*year*	*dm*	*s*	*increase*
(91)	1954	.14	2.83	7.03%
(92)	1954	.21	2.73	10.55%

Silverblu makes a large mink, larger than the Dark, but Moyle Buff is significantly larger than Silverblu. There is one comparison of males.

Appendix No.	*year*	*dm*	*s*	*increase*
(85)	1954	.69	9.86	20.60%

For females there is a similar comparison.

Appendix No.	*year*	*dm*	*s*	*increase*
(93)	1955	.12	3.58	5.77%

Moyle Buff is even larger than Pastel, No. (86), which is actually larger than Silverblu although direct comparisons cannot be made between Pastel and Silverblu. The reason is that Silverblu-Pastel is an unmarketable, dull greenish mink, and, consequently, ranchers avoid crossing their blood lines.

Appendix No.	*year*	*dm*	*s*	*increase*
(86)	1954	.25	4.7	6.60%

There is a comparison showing the significant size increasing effect of Moyle Buff on Silverblu-Aleutian. The dm is .13 pounds, the significance is 2.81, and the percentage increase is 3.47%.

An interesting comparison is No. (94). Here the effect of the Moyle Buff gene in the hybrid is compared with its effect in homozygous state. In both cases it is on a Silverblu background. The dm is .12, but the significance is not quite satisfactory.

Moyle Buff Hybrids

There are a number of comparisons demonstrating the large effect produced by inserting into animals one gene for Moyle Buff rather than two genes for Moyle Buff. Because the Moyle Buff coat color is a recessive, this dominant physiological effect on growth in the hybrid is of considerable interest.

To begin with, there is the comparison of hybrid Moyle Buff with normal Dark, comparison No. (99). The dm is .38, the

significance is 3.12, and the percentage increase is 9.64.

In comparison No. (100) Pastel males are smaller than Pastel hybrid for Moyle Buff. The dm is .17, and the significance of 1.79 is almost satisfactory.

In comparison No. (95) Silverblu males hybrid for Moyle Buff are significantly larger than Silverblu hybrid for Aleutian. It is known that the Aleutian gene in simplex makes little difference in the size of a mink. The dm is .52 pounds, and the significance is 4.9. The percentage boost of this gene in simplex is 12.52%.

There are several comparisons of male animals hybrid for Moyle Buff and similar phenotypes hybrid for certain other genes. In No. (96) two groups of Dark mink are compared. One group is hybrid for Moyle Buff and the other hybrid for both Ambergold, which tends to reduce, and Silverblu, which appears to be neutral in simplex. The dm is .62 pounds, the significance is 7.46. The percentage increase is 16.85%.

In comparison No. (106) Silverblu females hybrid for Moyle Buff are larger than Silverblu hybrid for Ambergold. The dm is small, being .07, and the significance of 1.21 is insignificant. The percentage increase is 3.30.

Probably comparison No. (106) is not significant since it represents very few animals. Comparison No. (107) is of a similar nature, but deals with larger populations. Here the dm is .40, the significance is 12.19. The percentage increase is 2.09.

In No. (97) are compared Silverblu hybrid for Moyle Buff and Silverblu hybrid for Palomino which, as shown above, might have a reducing effect. The dm is .84, the significance is 10.85, and the percentage increase is 25.30%.

Comparison No. (98) shows that Silverblu hybrid for Moyle Buff is significantly larger than Silverblu hybrid for Ambergold. The dm is .38, the significance is 6.95, and the percentage increase is 10.05%.

From the foregoing it might be expected that Aleutians hybrid for Moyle Buff would be larger than plain Aleutians. This is demonstrated in comparison No. (101). The dm is .18, the significance is 2.43, and the percentage increase is 4.85%.

In comparison No. (108) Dark females hybrid for Moyle Buff are compared with Aleutian hybrid for Moyle Buff. The booster effect on size made by the Moyle Buff gene in simplex is similar in both cases, so that the normal percentage decrease of Aleutian, when compared with Dark, is maintained. The dm is .21, the significance is 3.31. The percentage decrease is 10.00%.

Two curious comparisons, Nos. (102) and (103), are recorded, which may mean that the single Moyle Buff gene in the presence of two genes for Silverblu plus two genes for Aleutian, loses its power to increase size! These are comparisons of Silverblu-

Aleutian hybrid for Moyle Buff with Silverblu-Aleutian. In one case the dm is .07, and in the other .04, although the size differences are in the expected direction. The significance in both cases is very low.

The above is also interesting in view of comparison No. (104) in which Silverblu-Aleutian $_{A}^{hybrid}$ for Moyle Buff is very much larger than Silverblu-Aleutian hybrid for Ambergold which was shown to have a reducing effect on its hybrids. The dm is .47, the significance is 8.23, and the percentage increase is 14.16%.

A very interesting fact is demonstrated by comparison No. (105). A recessive mutation turned up which the investigators call Dark Moyle Allel. It makes a coat color with much of the color quality of Moyle, but darker. When it is crossed with Moyle Buff, instead of obtaining a Dark mink, one obtains an animal something like Moyle Buff or slightly darker. In the absence of evidence to the contrary, these two genes would appear to be alleles.

Curiously enough, however, the Dark Moyle Allel has little or no size influence on hybrids and none on purebreds.

In comparison No. (105) Moyle Buff males are compared with the Dark Moyle Allel. The dm is 1.18 pounds! The significance is 17.00! The percentage increase is 6.94.

Comparison No. (109) adds little of interest. It shows that Dark hybrid for Moyle Buff are larger than Dark hybrid for Ambergold and Silverblu. The dm is .18, the significance is 5.10, and the percentage increase is 8.45.

A similar effect on Aleutian is suggested in comparison No. (110). Aleutians carrying Moyle Buff in simplex are larger than Aleutians carrying one gene for Silverblu. The dm is .05, the significance is 1.27, and the percentage increase is 2.44.

Comparison (111) shows that when the purebred Dark strain has dropped in size because of the one error in selection, it may be identical in size with unselected, miscellaneous hybrids.

There are six genes for which measures of their effects are available, both in males and in females. In four of these the greatest effect is in the male, and in the other two it is in the female. However, the data are hardly sufficient to conclude that these genes actually have sex effects. Such effects conceivably can be due to errors of random sampling.

There are several genes the effects of which have been followed for twelve years (Chart 2.) During this time there has been found no evidence to indicate a change in the size effect of the coat color gene which might suggest linkage rather than pleiotropy. In the records all genes producing larger than normal size continued to do so (Moyle Buff, Silverblu, Pastel). All genes having a small size effect continued to produce a small size effect (Breath of Spring, Aleutian, Black Cross, Palomino, Ambergold).

THE BODY SIZE EFFECT OF VARIOUS MUTANTS IN PERCENT

Early Comparisons			Late Comparisons						
1946	1947	Others	1954	1955	1956	1957	1957	Total	
			7.03 / 10.55		17.85 10.93	12.44	3.47	10.41 / 8.79	Moyle Buff av. = 11.76% increase
5.1 / 8.6		8.2 / 11.13	6.53	4.63 / 12.56 7.80	14.45 7.73	8.12	5.53	7.70 / 0.31	Silverblu av = 8.38% increase
			4.52	8.17 10.41 3.80	13.33 12.75 / 5.55	5.84	6.84	8.73 / 5.03	Pastel av = 7.91% increase
1.0 / 0.6	3.2 / 3.3	9.0 3.0 / 5.2 1.9					5.86 4.98 1.83 5.00 1.41 4.98 5.00 1.47 2.88	3.91 / 2.78	Breath of Spring av = 3.50% decrease
5.1 / 8.9	6.4 / 7.2							5.75 / 8.05	Black Cross av = 6.90% decrease
			4.52	3.94 7.34 3.94 2.12 / 3.76	6.93		7.42 12.83 5.20 10.14 7.45 2.09 5.58 4.55 7.27	5.56 / 4.14	Aleutian av = 5.35% decrease
							16.44 10.98	13.71	Palomino av = 13.71% decrease
							10.40 9.68 11.74 13.46	11.32	Ambergold av — 11.32% decrease

TABLE 2. A list of mean body weights, represented in percent of standard Dark mink weight associated with sub-populations bearing simple coat colors, at the beginning and end of the twelve year period of study, to show relative constancy in amount and direction of the deviations. Data for males are at the upper left of the rectangles; data for females at the lower right.

In combination through twelve years Breath of Spring combined to reduce the plus effect of Silverblu in animals manifesting both Breath of Spring and Silverblu genes.

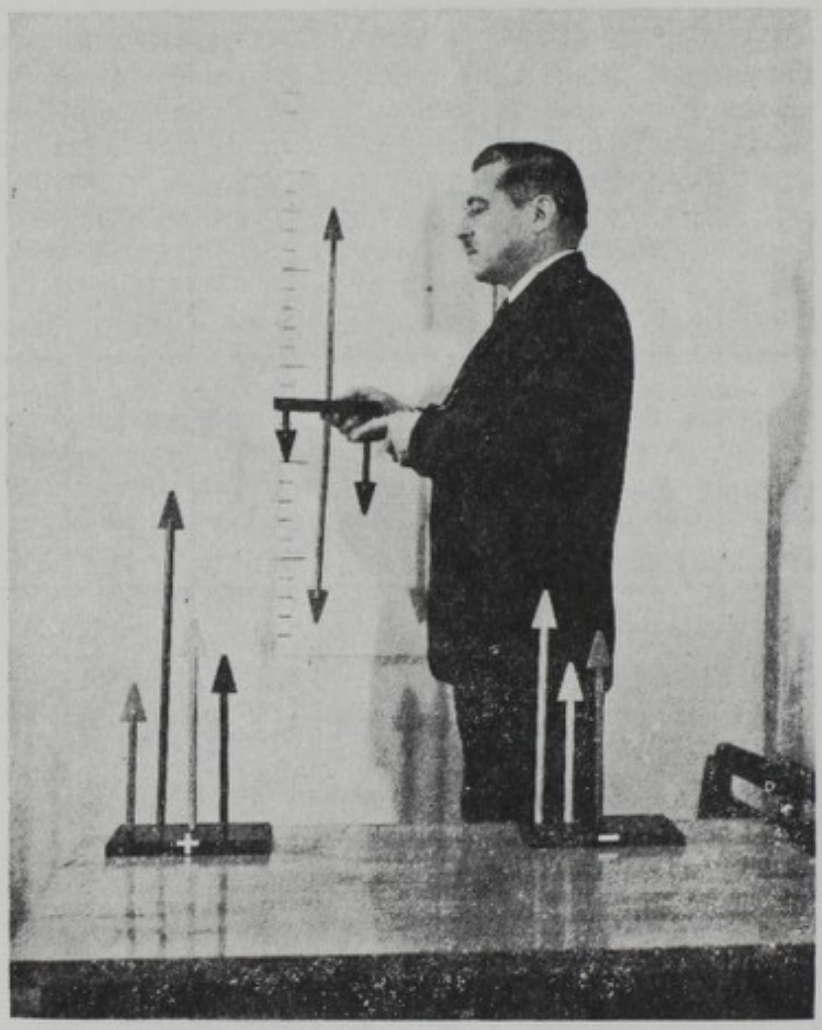


FIGURE 1. *Wooden vector-models to illustrate the plus or minus size effects of the various coat color genes of mink included in this study. The vector quantities representing increaser or decreaser effects are in percentage of the mean size of normal Dark mink taken as 100%. The assembled model illustrates the interaction between Breath of Spring, Silverblu, Aleutian, and Palomino genes resulting in a mink smaller than normal size.*

If the present interpretation is correct, then the effects of the coat color genes studied may be represented as vector quantities, directed either upward or downward from a horizontal line representing quantitatively the position of the normal mean.

If the horizontal line of the normal mean is represented by a long block of wood pierced with holes, and the vector quantities represented by wooden arrows, the rear ends of the shafts of which fit snugly into these holes, then visual models of the forces acting on size in each genetic combination may be constructed. Such models allow visualization of these growth forces much as molecular models assist the chemist to comprehend the relative positions of the interacting atoms; see Figure 1. In addition, they permit comparison of genetic combinations in terms of percentage, thus giving a common unit of comparisons not available in terms of the actual weights, due to sex differences and the general annual selection for larger size which was effective upon genes not tagged by means of coat color modifications.

The genetic models of 45 combinations of genes from late comparisons were prepared and are presented in five charts in which the difference between the means of the populations was found to be significant. Those comparisons are listed in the Appendix and are referred to by letters of the alphabet. See Charts 3, 4, 5, 6, 7. An examination of these comparisons between models will reveal that none are inconsistent with the interpretation given to the various size tendencies and their interactions described in this paper.

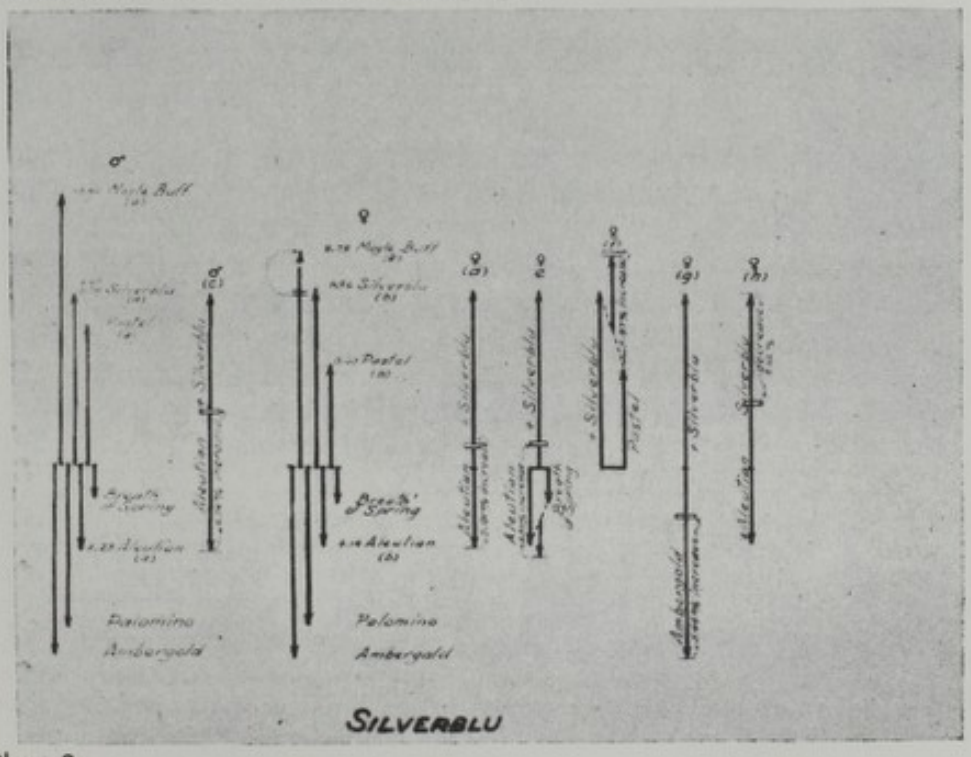


Chart 3.

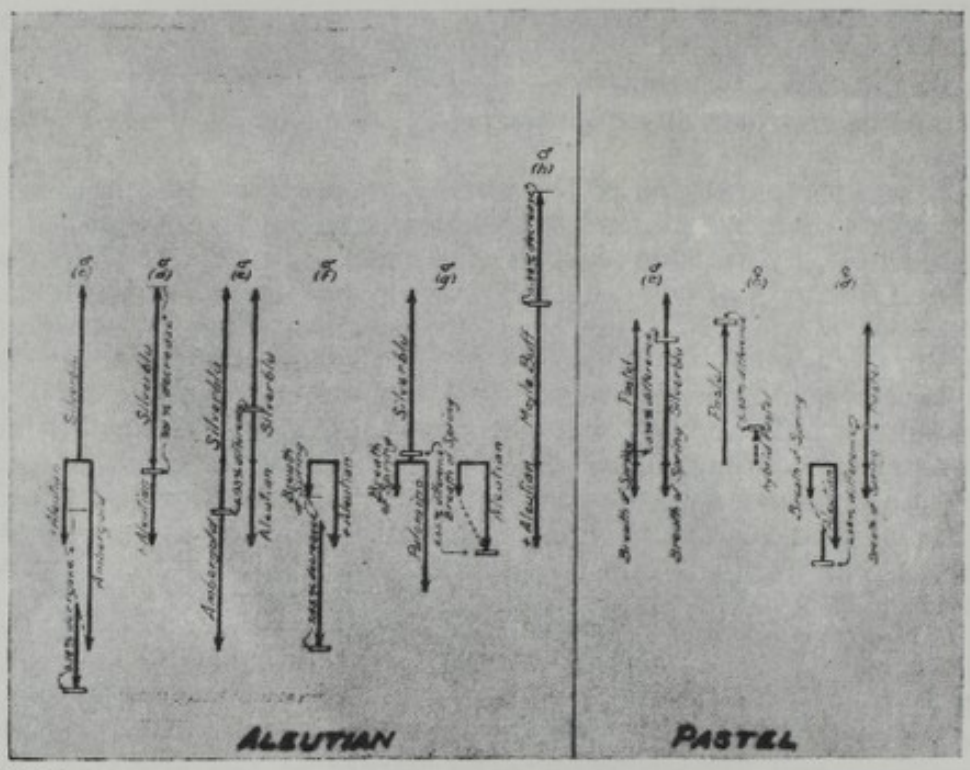


Chart 4.

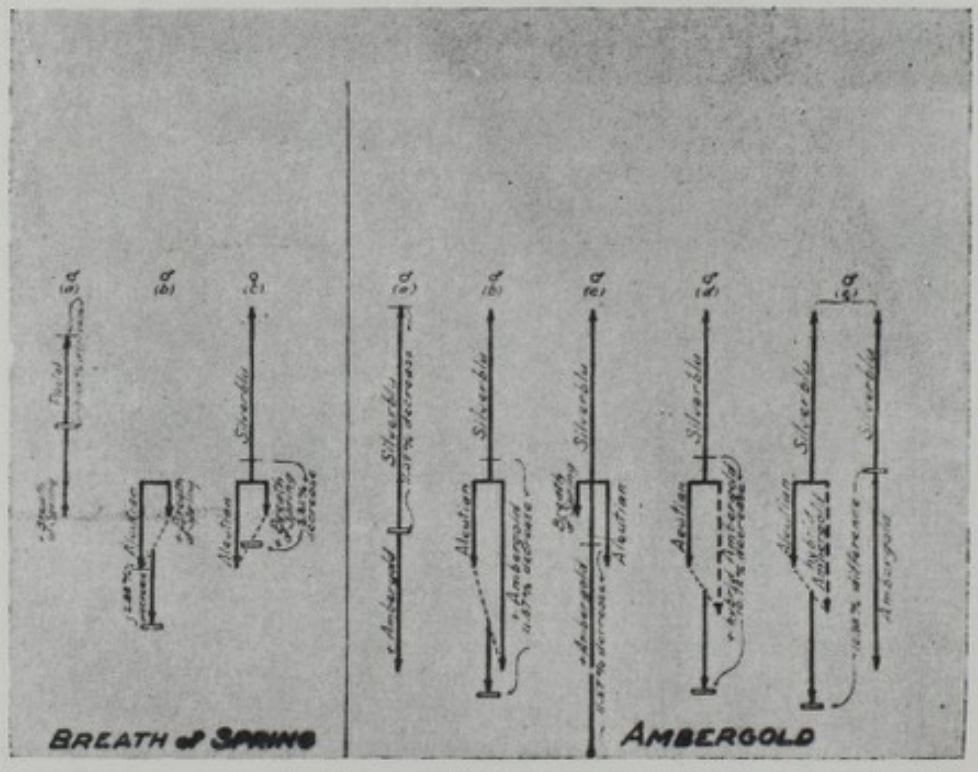


Chart 5.

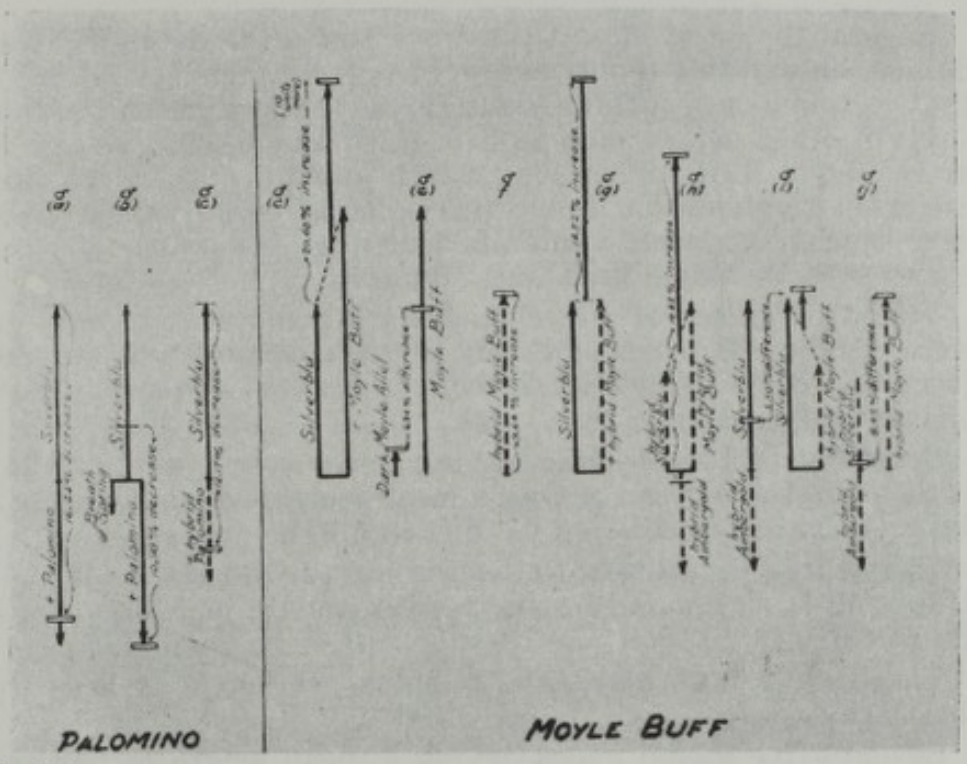


Chart 6.

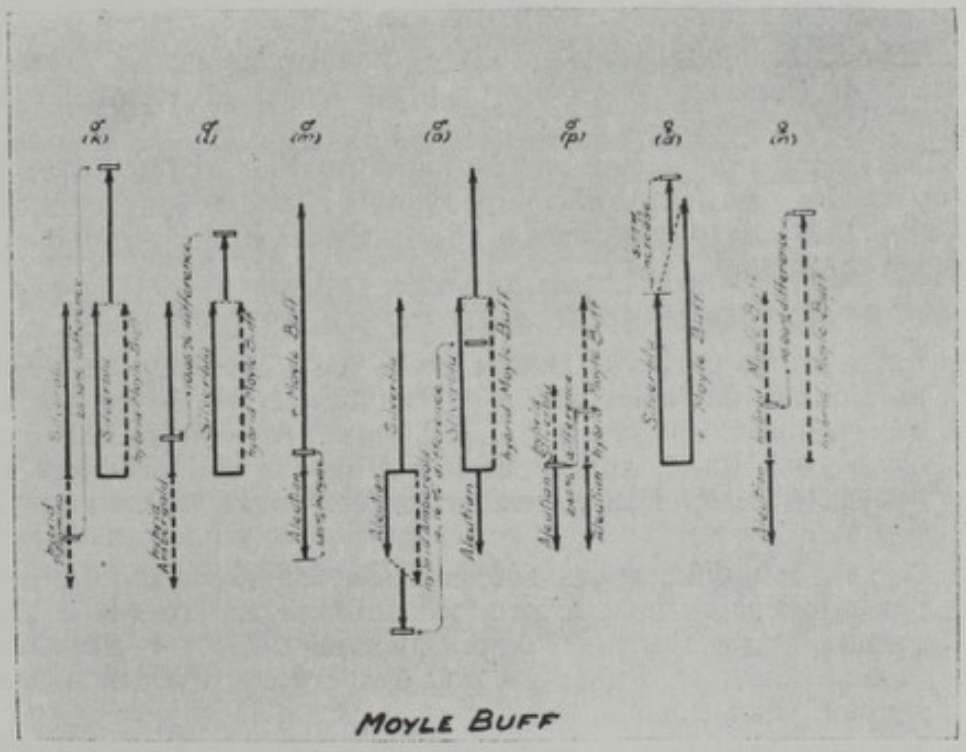


CHART 7. *Charts 3, 4, 5, 6, 7. Vector quantity models representing the growth tendencies of certain coat color constitutions of mink and their comparisons as listed in the index under the title of "Late Comparisons,"*

Several thousand dissections were made, the details of which do not concern this report except that from them it was learned that certain genes, such as Aleutian, make short, slender animals. Certain other genes, such as Silverblu, make large, stocky animals. Moyle Buff makes long, large animals. The Moyle Buff-Silverblu combination is enormous, being both very large and very stocky, apparently manifesting the size and shape tendencies of both Moyle Buff and Silverblu.

Pelted carcasses of Pastel and Dark mink of the 1947 crop were weighed in grams and body length measured in millimeters (nose to rump). The Pastels, both males and f. nales, are significantly larger than the Darks.

Seventy-five Pastel males having a mean weight of 975.24 ± 17.88 > 52 Dark males having a mean weight of 924.30 ± 16.95. dm = 50.94 ± 24.64. s = 2.07. diff = 5.23%.

Fifty-three Pastel females having a mean weight of 587.66 ± 8.30 > 50 Dark females having a mean weight of 543.96 ± 6.55. dm = 43.70 ± 10.57. s = 4.13. diff = 7.44%.

The Pastels, both males and females, are longer in body than the Darks.

Seventy-five Pastel males having a mean length of 592.98 ± 3.04 > 52 Dark males having a mean length of 572.34 ± 5.01. dm = 20.64 ± 5.86. s = 3.52. diff. = 3.38%.

Fifty-three Pastel females having a mean length of 502.52 ± 4.25 > 49 Dark females having a mean length of 508.55 ± 3.55. dm = 6.03 ± 5.54. s = 1.09. diff = 1.19%.

The length comparison on this small number of females is not statistically significant although Pastels are 1.19% shorter than Darks. The length comparison shows Pastel males significantly longer than Dark males.

DISCUSSION AND CONCLUSIONS

1. Since over a period of twelve years the correlation between a particular coat color and a particular size tendency has not been found to change, it appears most probable that the coat color gene itself, rather than a linked gene, produces the associated size tendency, either large or small in the material studied.
2. Certain coat color genes, such as those for Moyle Buff, Silverblu, and Pastel, tend to produce animals of larger size than normal Dark. Certain others, such as those for Breath of Spring, Aleutian, Palomino, and Ambergold, produce animals smaller than normal.
3. The size tendency of each coat color gene is manifested in both males and females, although there are marked differences in body weight between the two sexes because of sex factors.

4. Heterozygosity for various coat colors may produce detectable effects on body size. Breath of Spring is due to a dominant gene, lethal in the homozygous state. The other genes dealt with are recessives, and of these, Moyle Buff, Palomino, and Ambergold manifest effects on body size in the heterozygote.
5. Two large-size genes in the same animal in homozygous state tend to produce animals still larger than would be produced by either gene alone. However, this is accompanied by a discount, since the resultant size is never quite equal to the sum of the increases made by the two genes acting alone.
6. Two small size genes tend to produce animals smaller than would be produced by either gene alone. Here again, the reduction is not as great as the sum of the reductions made by the two genes acting alone.
7. The effects of genes making for larger than normal size tend to be neutralized by the effects of genes making for smaller than normal size.
8. A certain gene for small size may act differently in combination with a certain large-size gene than in combination with another certain gene for large size.
9. It was observed that certain genes, such as Aleutian, tend to make short, slender animals. Others, such as Silverblu, tend to produce large, stocky animals. Moyle Buff tends to make long, large animals. The combination between Silverblu and Moyle Buff produces animals both long and stocky, apparently manifesting the outstanding tendencies of both genes.

Thus, it may be concluded that a study of body length and body shape would reveal certain lengths and proportions associated with certain genes and manifesting themselves in combinations of these genes in much the same fashion that body weight does.

SUMMARY

A statistical study of weight data was made over a period of twelve years upon a population of over 100,000 ranch-bred mink. This study revealed that certain coat color genes tend to produce larger than normal Dark body size (weight) and that others tend to produce smaller than normal body size. These size effects tend to be somewhat additive (when the plus and minus signs are respected) in that two plus genes in the same animal make it still larger, two minus genes make it still smaller, and a plus gene in combination with a minus gene tends to cancel out their size deviations from normal. Some size tendencies of coat color genes are detectable in heterozygotes.

ACKNOWLEDGEMENT

The author is indebted to Larry Moore and the staff of his mink ranch for their generous cooperation on this problem for more than a decade. He is grateful to Sir Ronald Fisher with whom he discussed the adequacy for this material of the simple statistical method of analysis employed.

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APPENDIX

COMPARISON OF BODY WEIGHTS OF SUB-POPULATIONS SEGREGATING FOR COAT COLOR

dm is difference between means. s is "Significance" which represents the difference between means divided by the standard error of the difference betwen the means. diff is difference in percent.

Early Comparisons

SILVERBLU MALES

(1) *Silverblu 1946.* 584 Silverblu mean 3.32 ± .024 > 189 Dark mean 3.15 ± 0.35. dm = .17 ± .042. s = 4.0. diff = 5.1%.

(2) *Silverblu 1946.* 584 Silverblu mean 3.32 ± .024 > 292 Breath of Spring-Silverblu mean 3.29 ± .023. dm = .03 ± .033. s = 0.9. diff = 0.9%.

(3) *Silverblu 1946.* 534 Silverblu mean 3.32 ± .024 > 149 Breath of Spring mean 3.02 ± .037. dm = .30 ± .044. s = 6.8. diff = 9.0%.

(4) *Silverblu 1946.* 584 Silverblu mean 3.32 ± .024 > 188 Black Cross mean 2.99 ± .035. dm = .33 ± .042. s = 7.8. diff = 10.0%.

(5) *Silverblu 1947.* 537 Silverblu mean 3.42 ± .025 < 266 Dark mean 3.43 ± .035. dm = .01 ± .043. s = 0.23. diff = 0.3%.

(6) *Silverblu 1947.* 537 Silverblu mean 3.42 ± .025 > 473 Breath of Spring-Silverblu mean 3.32 ± .025. dm = .10 ± .035. s = 2.86. diff = 3.0%.

(7) *Silverblu 1947.* 537 Silverblu mean 3.42 ± .025 > 28 Breath of Spring mean 3.20 ± .097. dm = .22 ± .100. s = 2.2. diff = 6.4%.

(8) *Silverblu 1947.* 537 Silverblu mean 3.42 ± .025 > 54 Black Cross mean 3.21 ± .063. dm = .21 ± .068. s = 3.08. diff = 6.2%.

SILVERBLU FEMALES

(9) *Silverblu 1946.* 511 Silverblu mean 2.10 ± .004 > 185 Dark mean 1.92 ± .016. dm = .18 ± .016. s = 11.2. diff = 8.6%.

(10) *Silverblu 1946.* 511 Silverblu mean 2.10 ± .004 > 273 Breath of Spring-Silver mean 1.99 ± .018. dm = .11 ± .018. s = 6.1. diff = 5.2%.

(11) *Silverblu 1946.* 511 Silverblu mean 2.10 ± .004 > 133 Breath of Spring mean 1.77 ± .017. dm = .33 ± .017. s = 19.4. diff = 5.7%.

(12) *Silverblu 1946.* 511 Silverblu mean 2.10 ± .004 > 193 Black Cross mean 1.76 ± .015. dm = .34 ± .015. s = 22.7. diff = 6.2%.

(13) *Silverblu 1947.* 527 Silverblu mean 2.10 ± .014 > 216 Dark mean 2.08 ± .017. dm = .03 ± .022. s = 1.36. diff = 1.0%.

(14) *Silverblu 1947.* 527 Silverblu mean 2.10 ± .014 > 394 Breath of Spring-Silverblu mean 2.06 ± .015. dm = .04 ± .020. s = 2.0. diff = 1.9%.

(15) *Silverblu 1947.* 527 Silverblu mean 2.10 ± .014 > 16 Breath of Spring mean 1.95 ± .067. dm = .15 ± .068. s = 2.20. diff = 7.2%.

(16) *Silverblu 1947.* 527 Silverblu mean 2.10 ± .014 > 44 Black Cross mean 1.93 ± .028. dm = .17 ± .083. s = 2.05. diff = 8.1%.

BREATH OF SPRING MALES

(17) *Breath of Spring 1946.* 149 Breath of Spring mean 3.02 ± .037 > 188 Black Cross mean 2.99 ± .035. dm = .03 ± .051. s = 0.6. diff = 1.0%.

(18) *Breath of Spring 1496.* 189 Dark mean 3.15 ± .035 > 149 Breath of Spring mean 3.02 ± .037. dm = .13 ± .051. s = 2.5. diff = 4.2%.

(19) *Breath of Spring 1947.* 473 Breath of Spring mean 3.32 ± .025 < Dark mean 3.43 ± .035. dm = .11 ± .045. s = 2.44. diff = 3.2%.

(20) *Breath of Spring 1947.* 473 Breath of Spring mean 3.32 ± .025 > 54 Black Cross mean 3.21 ± .063. dm = .11 ± .068. s = 1.62. diff = 3.3%.

BREATH OF SPRING FEMALES

(21) *Breath of Spring 1946.* 133 Breath of Spring mean 1.77 ± .017 > 193 Black Cross mean 1.76 ± .015. dm = .01 ± .023. s = 0.4. diff = 0.6%.

BREATH OF SPRING MALES

(22) *Breath of Spring 1946.* 185 Dark mean 1.92 ± .016 > 133 Breath of Spring mean 1.77 ± .017. dm = .15 ± .023. s = 6.5. diff = 7.8%.

(23) *Breath of Spring 1947.* 394 Breath of Spring mean 2.06 ± .015 < 216 Dark mean 2.08 ± .017. dm = .02 ± .023. s = 0.87. diff = 1.0%.

(24) *Breath of Spring 1947.* 394 Breath of Spring mean 2.06 ± .015 > 44 Black Cross mean 1.93 ± .028. dm = .13 ± .032. s = 4.06. diff = 6.3%.

BREATH OF SPRING-SILVERBLU MALES

(25) *Breath of Spring-Silverblu 1946.* 292 Breath of Spring-Silverblu mean 3.29 ± .023 > 189 Dark mean 3.15 ± .035. dm = .14 ± .042. s = 3.3. diff = 4.3%.

(26) *Breath of Spring-Silverblu 1946.* 292 Breath of Spring-Silverblu mean 3.29 ± .023 > 149 Breath of Spring mean 3.02 ± .037. dm = .27 ± .043. s = 6.3. diff = 8.2%.

(27) *Breath of Spring-Silverblu 1946.* 292 Breath of Spring-Silverblu mean 3.29 ± .023 > 188 Black Cross mean 2.99 ± .035. dm = .30 ± .042. s = 7.1. diff = 8.1%.

(28) *Breath of Spring-Silverblu 1947.* 473 Breath of Spring-Silverblu mean 3.32 ± .025 < 266 Dark mean 3.43 ± .025. dm = .11 ± .035. s = 3.14. diff = 3.2%.

(29) *Breath of Spring-Silverblu 1947.* 473 Breath of Spring-Silverblu mean 3.32 ± .025 > 28 Breath of Spring mean 3.20 ± .097. dm = .12 ± .100. s = 1.2. diff = 3.6%.

(30) *Breath of Spring-Silverblu 1947.* 473 Breath of Spring-Silverblu mean 3.32 ± .025 > 54 Black Cross mean 3.21 ± .063. dm = .11 ± .068. s = 1.62. diff = 3.3%.

BREATH OF SPRING-SILVERBLU FEMALES

(31) *Breath of Spring-Silverblu 1946.* 273 Breath of Spring-Silverblu mean 1.99 ± .018 > 185 Dark mean 1.92 ± .016. dm = .07 ± .024. s = 2.9. diff = 3.5%.

(32) *Breath of Spring-Silverblu 1946.* 273 Breath of Spring-Silverblu mean 1.99 ± .018 > 133 Breath of Spring mean 1.77 ± .017. dm = .22 ± .025. s = 8.8. diff = 11.1%.

(33) *Breath of Spring-Silverblu 1946.* 273 Breath of Spring-Silverblu mean 1.99 ± .018 > 193 Black Cross mean 1.76 ± .015. dm = .23 ± .024. s = 9.16. diff = 11.6%.

(34) *Breath of Spring-Silverblu 1947.* 394 Breath of Spring-Silverblu mean 2.06 ± .015 < 216 Dark mean 2.08 ± .017. dm = .02 ± .023. s = 0.87. diff = 1.0%.

(35) *Breath of Spring-Silverblu 1947.* 394 Breath of Spring-Silverblu mean 2.06 ± .015 > 16 Breath of Spring mean 1.95 ± .067. dm = .11 ± .069. s = 1.59. diff = 5.3%.

(36) *Breath of Spring-Silverblu 1947.* 394 Breath of Spring-Silverblu mean 2.06 ± .015 > 44 Black Cross mean 1.93 ± .028. dm = .13 ± .032. s = 4.06. diff = 6.3%.

BLACK CROSS MALES

(37) *Black Cross 1946.* 189 Dark mean 3.15 ± .035 > 188 Black Cross mean 2.99 ± .035. dm = .16 ± .038. s = 4.2. diff = 5.1%.

(38) *Black Cross 1947.* 54 Black Cross mean 3.21 ± .063 < 266 Dark mean 3.43 ± .035. dm = .22 ± .072. s = 3.05. diff = 6.4%.

BLACK CROSS FEMALES

(39) *Black Cross 1946.* 185 Dark mean 1.92 ± .016 > 193 Black Cross mean 1.75 ± .015. dm = .16 ± .022. s = 7.3. diff = 8.9%.

(40) *Black Cross 1947.* 44 Black Cross mean 1.93 ± .028 < 216 Dark mean 2.08 ± .017. dm = .15 ± .033. s = 4.54. diff = 7.2%.

LATE COMPARISONS

SILVERBLU MALES

(1) *Silverblu 1954.* 470 Silverblu-Aleutian mean 3.28 ± .0214 > 111 Aleutian (hybrid for Silverblu) mean 3.16 ± .0319. dm = .12 ± .0384. s = 3.1.

(2) *Silverblu 1954.* 422 Silverblu-Breath of Spring-Aleutian mean 3.22 ± .0208 > 115 Breath of Spring-Aleutian (hybrid for Silverblu) mean 3.16 ± .0319. dm = .06 ± .0381. s = 1.57.

(3) *Silverblu 1954.* 49 Silverblu (hybrid for Moyle Buff) mean 3.87 ± .0804 > 191 Dark (hybrid for Moyle Buff) mean 3.85 ± .0503. dm = .02 ± .0948. s = 0.21.

(4) *Silverblu 1955.* 191 Silverblu (carry Ambergold) mean 3.78 ± .0345 > 42 Dark (wild type) mean 3.55 ± .0706. dm = .23 ± .0785. s = 2.93.

(5) *Silverblu 1956.* 23 Silverblu mean 4.04 ± .1465 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920. dm = .51 ± .1729. s = 2.88.

(6) *Silverblu 1956.* 23 Silverblu mean 4.04 ± .1465 > 10 Dark (wild type) mean 3.94 ± .0967. dm = .32 ± .0936. s = 1.42.

(7) *Silverblu 1957.* 19 Silverblu mean 4.26 ± .0646 > 27 Dark (wild type) mean 3.94 ± .0967. dm = .32 ± .9036. s = 3.43.

SILVERBLU FEMALES

(8) *Silverblu 1954.* 67 Silverblu (hybrid for Aleutian) mean 2.20 ± .0541 > 208 Pastel mean 2.08 ± .0182. dm = .12 ± .0571. s = 2.10.

(9) *Silverblu 1954.* 25 Silverblu mean 2.12 ± .0428 = 37 Breath of Spring-Silverblu (hybrid for Aleutian) mean 2.12 ± .0476. no dm.

(10) *Silverblu 1954.* 67 Silverblu (hybrid for Aleutian) mean 2.20 ± .0541 > 37 Breath of Spring-Silverblu (hybrid for Aleutian) mean 2.12 ± .0476. dm = .08 ± .0720. s = 1.1.

(11) *Silverblu 1954.* 67 Silverblu (hybrid for Aleutian) mean 2.20 ± .0541 > 168 Aleutian (hybrid for Silverblu) mean 2.08 ± .0164. dm = .12 ± .0559. s = 2.15.

(12) *Silverblu 1954.* 453 Silverblu-Aleutian mean 2.04 ± .0127 < 168 Aleutian (hybrid for Silverblu) mean 2.08 ± .0160. dm = .04 ± .0204. s = 1.96.

(13) *Silverblu 1954.* 37 Silverblu-Breath of Spring (hybrid for Aleutian) mean 2.12 ± .0476 > 177 Pastel-Breath of Spring mean 2.08 ± .0191. dm = .04 ± .0513. s = .08.

(14) *Silverblu 1954.* 325 Silverblu-Breath of Spring-Aleutian mean 2.01 < 87 Breath of Spring-Aleutian (hybrid for Silverblu) mean 2.02 ± .0253. dm = .01 ± .0292. s = .03.

(15) *Silverblu 1954.* 25 Silverblu (hybrid for Ambergold) mean 2.12 ± .0428 > Dark mean 1.99 ± .0272. dm = .13 ± .0507. s = 2.56.

(16) *Silverblu 1955.* 190 Silverblu (hybrid for Ambergold) mean 2.15 ± .0203 > 77 Dark (hybrid for Silverblu and Ambergold) 1.91 ± .0290. dm = .24 ± .0354. s = 6.78.

(17) *Silverblu 1955.* 158 Silverblu-Ambergold mean 2.13 ± .0205 > 141 Dark (hybrid for Ambergold and Silverblu) mean 2.02 ± .0228. dm = .11 ± .0300. s = 3.66.

(18) *Silverblu 1955.* 190 Silverblu (hybrid for Ambergold) mean 2.15 ± .0203 > 141 Dark (hybrid for Silverblu and Ambergold) mean 2.02 ± .0228. dm = .13 ± .0305. s = 4.26.

(19) *Silverblu 1955.* 157 Silverblu-Aleutian mean 2.21 ± .0216 > 80 Aleutian mean 2.05 ± .0277. dm = .16 ± .0351. s = 1.56.

(20) *Silverblu 1955.* 136 Silverblu-Breath of Spring-Aleutian mean 2.10 ± .0233 > 56 Breath of Spring-Aleutian (hybrid for Silverblu) mean 1.99 ± .0296. dm = .11 ± .0376. s = 2.92.

(21) *Silverblu 1956.* 213 Silverblu-Aleutian mean 2.03 ± .0137 > 145 Aleutian mean 2.00 ± .0167. dm = .03 ± .0216. s = 1.39.

(22) *Silverblu 1956.* 64 Silverblu-Moyle Buff mean 2.15 ± .0319 > 418 Moyle Buff mean 2.09 ± .0120. dm = .06 ± .0341. s = 1.76.

ALEUTIAN MALES

(23) *Aleutian 1954.* 422 Aleutian-Breath of Spring-Silverblu mean 3.22 ± .0208 < 37 Breath of Spring-Silverblu mean 3.46 ± .0652. dm = .24 ± .0680. s = 3.5.

(24) *Aleutian 1954.* 422 Aleutian-Breath of Spring-Silverblu mean 3.08 ± .0332 < 184 Breath of Spring-Silverblu-Palomino mean 3.22 ± .0208. dm = .14 ± .0392. s = 3.6. Aleutian reduces more than Palomino.

(25) *Aleutian 1954.* 470 Aleutian-Silverblu mean 3.28 ± .0214 < 37 Silverblu (hybrid for Aleutian) mean 3.46 ± .0652. dm = .18 ± .0498. s = 3.61.

(26) *Aleutian 1954.* 470 Aleutian-Silverblu mean 3.28 ± .0214 < Silverblu mean 3.35 ± .0681. dm = .07 ± .0713. s = 1.0.

(27) *Aleutian 1955.* 191 Silverblu (hybrid for Ambergold) mean 3.78 ± .0345 > 13 Silverblu-Aleutian mean 3.35 ± .0468. dm = .43 ± .0581. s = 7.40.

(28) *Aleutian 1955.* 42 Dark (wild type) mean 3.55 ± .0766 > 98 Aleutian (hybrid for Silverblu) mean 3.49 ± .0495. dm = .14 ± .0866. s = 0.70.

(29) *Aleutian 1955.* 42 Dark (wild type) mean 3.55 ± .0766 > 108 Aleutian (hybrid for Silverblu) mean 3.41 ± .0503. dm = .14 ± .0866. s = 1.62.

(30) *Aleutian 1955.* 43 Dark (hybrid for Silverblu and Ambergold) mean 3.68 ± .0745 > 98 Aleutian (hybrid for Silverblu) mean 3.49 ± .0495. dm = .19 ± .0894. s = 2.12.

(31) *Aleutian 1955.* 43 Dark (hybrid for Silverblu and Ambergold) mean 3.68 ± .0745 > 108 Aleutian (hybrid for Silverblu) mean 3.41 ± .0503. dm = .27 ± .0893. s = 3.02.

(32) *Aleutian 1956.* 10 Dark (wild type) mean 3.75 ± .1413 > 254 Aleutian (hybrid for other genes) mean 3.49 ± .0308. dm = .26 ± .1446. s = 1.80.

(33) *Aleutian 1956.* 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920 > 254 Aleutian (hybrid for other genes) mean 3.49 ± .0308. dm = .04 ± .0959. s = 0.42.

(34) *Aleutian 1956.* 348 Silverblu-Ambergold mean 3.62 ± .0269 > 73 Silverblu-Ambergold-Aleutian mean 3.37 ± .0491. dm = .25 ± .0559. s = 4.47.

(35) *Aleutian 1957.* 236 B of S-Silverblu-Ambergold mean 3.65 ± .0312 > 95 B of S-Silverblu-Ambergold-Aleutian mean 3.28 ± .0382. dm = .37 ± .0493. s = 7.90.

ALEUTIAN FEMALES

(36) *Aleutian 1954.* 453 Aleutian-Silverblu mean 2.04 ± .0127 < 67 Silverblu (hybrid for Aleutian) mean 2.20 ± .0541. dm = .16 ± .0556. s = 2.88.

(37) *Aleutian 1954.* 453 Aleutian-Silverblu mean 2.04 ± .0127 < 25 Silverblu (hybrid for Ambergold) mean 2.12 ± .0428. dm = .08 ± .0446. s = 1.79.

(38) *Aleutian 1954.* 168 Aleutian (hybrid for Silverblu) mean 2.08 ± .0164 < 49 Dark mean 1.99 ± .0272. dm = .09 ± .0164. s = 2.83.

(39) *Hybrid Aleutian 1954.* 67 Silverblu (hybrid for Aleutian) mean 2.20 ± .0541 > 25 Silverblu (hybrid for Ambergold) mean 2.12 ± .0428. dm = .08 ± .0690. s = 1.16.

(40) *Aleutian 1955.* 80 Aleutian (hybrid for Silverblu) mean 2.05 ± .0277 < 65 Dark (hybrid for Ambergold and Silverblu) mean 2.13 ± .0318. dm = .8. s = 1.89.

(41) *Aleutian 1955.* 77 Aleutian-Silverblu-Breath of Spring mean 3.40 ± .0513 < 141 Silverblu-Ambergold-Breath of Spring mean 3.41 ± .0387. dm = .01 ± .0642. s = .15.

(42) *Aleutian 1956.* 56 Aleutian-Moyle Buff-Silverblu mean 2.03 ± .0323 < 64 Moyle Buff-Silverblu mean 2.15 ± .0319. dm = .12 ± .0323. s = 2.64.

(43) *Aleutian 1956.* 213 Aleutian-Silverblu mean 2.03 ± .0137 > 301 Silverblu-Ambergold mean 1.93 ± .0154. dm = .10 ± .0206. s = 4.85.

PASTEL MALES

(44) *Pastel 1954.* 154 Pastel-Breath of Spring mean 3.58 ± .0450 > 37 Breath of Spring-Silverblu mean 3.46 ± .0652. dm = .12. s = 1.51.

(45) *Pastel 1955.* 48 Pastel-Breath of Spring mean 3.80 ± .0617 > 23 Breath of Spring mean 4.04 ± .1465. dm = .24. s = .15.

(46) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 42 Dark (wild type) mean 3.55 ± .0706. dm = .29 ± .0787. s = 3.68.

(47) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 71 Dark (hybrid for Ambergold) mean 3.46 ± .0659. dm = .36 ± .0743. s = 4.84.

(48) *Pastel 1955.* 238 Pastel mean 3.84 ± .0345 > 43 Dark (hybrid for Ambergold and Silverblu) mean 3.68 ± .0745. dm = .14 ± .0820. s = 1.71.

(49) *Pastel 1956.* 534 Pastel mean 4.25 ± .0213 > 10 Dark (wild type) mean 3.75 ± .1413. dm = .50 ± .1428. s = 3.50.

(50) *Pastel 1956.* 152 Pastel (hybrid for B of S) mean 3.98 ± .0455 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920. dm = .45 ± .1020. s = 4.40.

(51) *Pastel 1957.* 222 Pastel mean 4.17 ± .0411 > 27 Dark (wild type) mean 3.94 ± .0967. dm = .23 ± .1057. s = 2.17.

(52) *Pastel 1954.* 208 Pastel mean 2.08 ± .0182 > 49 Dark mean 1.99 ± .0272. dm = .09 ± .0327. s = 2.75.

(53) *Pastel 1956.* 400 Pastel mean 2.04 ± .0138 < 364 Dark (hybrid for Pastel) mean 2.16 ± .0131. dm = .12 ± .0190. s = 6.31.

(54) *Pastel 1956.* 152 Pastel-Blufrost mean 2.03 ± .0258 > 54 Blufrost-Aleutian mean 1.90 ± .0336. dm = .13 ± .0424. s = 3.06.

(55) *Hybrid Pastel 1956.* 364 Dark (hybrid for Pastel) mean 2.16 ± .0131 > 19 Dark mean 2.01 ± .0480. dm = .15 ± .0497. s = 3.02.

BREATH OF SPRING MALES

(56) *Breath of Spring 1954.* 115 Breath of Spring-Aleutian (hybrid for Silverblu) mean 3.16 ± .0319 < 111 Aleutian (hybrid for Silverblu) mean 3.21 ± .0355. dm = .05 ± .0462. s = 1.1.

(57) *Breath of Spring 1954.* 422 Breath of Spring-Silverblu-Aleutian mean 3.22 ± .0208 < 470 Silverblu-Aleutian mean 3.28 ± .0214. dm = .06 ± .0299. s = 2.0.

(58) *Breath of Spring 1954.* 37 Breath of Spring-Silverblu (hybrid for Aleutian) mean 3.46 ± .0652 < 56 Silverblu (hybrid for Aleutian) mean 3.35 ± .0509. dm = .11 ± .5140. s = 2.14.

(59) *Breath of Spring 1954.* 154 Breath of Spring-Pastel mean 3.58 ± .0450 < 119 Pastel mean 3.79 ± .0511. dm = .21 ± .0680. s = 3.1.

(60) *Breath of Spring 1955.* 48 Breath of Spring-Pastel mean 3.80 ± .0617 < 238 Pastel mean 3.82 ± .0345. dm = .02 ± .0707. s = .28.

(61) *Breath of Spring 1955.* 77 Breath of Spring-Silverblu-Aleutian mean 3.40 ± .0513 > 13 Silverblu-Aleutian mean 3.35 ± .0468. dm = .05 ± .0694. s = .72.

(62) *Breath of Spring 1956.* 23 B of S mean 4.04 ± .1465 > 19 Silverblu-B of S mean 3.90 ± .1100. dm = .14 ± .1832. s = 0.76.

(63) *Breath of Spring Hybrids 1956*.....534 Pastel mean 4.25 ± .0213 > 152 Pastel (hybrid for Breath of Spring) mean 3.98 ± .0455. dm = .27 ± .0228. s = 11.84.

(64) *Breath of Spring 1957.* 222 Pastel mean 4.17 ± .0411 > 13 B of S mean 3.88 ± .1130. dm = .23 ± .1057. s = 6.81.

BREATH OF SPRING FEMALES

(65) *Breath of Spring 1954.* 325 Breath of Spring-Silverblu-Aleutian mean 2.01 ± .0145 < 453 Silverblu-Aleutian mean 2.04 ± .0127. dm = .03 ± .0193. s = 1.55.

(66) *Breath of Spring 1954.* 177 Breath of Spring-Pastel mean 2.08 ± .0191 = 208 Pastel mean 2.08 ± .0182. no dm.

(67) *Breath of Spring 1954.* 87 Breath of Spring-Aleutian (hybrid for Silverblu) mean 2.02 ± .0253 < 168 Aleutian (hybrid for Silverblu) mean 2.08 ± .0164. dm = .06 ± .0301. s = 1.99.

(68) *Breath of Spring 1955.* 56 Breath of Spring-Aleutian (hybrid for Silverblu) mean 1.99 ± .0296. dm = .06 ± .0296. s = 1.61.

(69) *Breath of Spring 1955.* 136 Breath of Spring-Silverblu-Aleutian mean 2.10 ± .0233 < 157 Silverblu-Aleutian mean 2.21 ± .0216. dm = .11 ± .0317. s = 3.47.

(70) *Breath of Spring 1955.* 71 Breath of Spring-Pastel mean 2.08 ± .0321 > 253 Pastel mean 2.02 ± .0194. dm = .06 ± .0321. s = 1.87.

(71) *Breath of Spring 1955.* 77 Breath of Spring-Silverblu-Aleutian mean 3.40 ± .0513 > 131 Silverblu-Aleutian mean 3.35 ± .0468. dm = .05 ± .0694. s = 0.72.

(72) *Breath of Spring 1956.* 152 Breath of Spring-Pastel mean 2.03 ± .0258 < 400 Pastel mean 2.04 ± .0138. dm = .01 ± .0292. s = 0.30.

(73) *Breath of Spring 1956.* 54 Breath of Spring-Aleutian (hybrid for Ambergold) mean 1.90 ± .0336 < 145 Aleutian mean 2.00 ± .0167. dm = .10 ± .0375. s = 2.67.

AMBERGOLD MALES

(74) *Ambergold 1956.* 23 Silverblu mean 4.04 ± .1465 > 348 Silverblu-Ambergold mean 3.62 ± .0269. dm = .42 ± .1489. s = 2.82.

(75) *Ambergold Hybrids 1955.* 42 Dark (wild type) mean 3.55 ± .0706 >71 Dark (hybrid for Ambergold) mean 3.46 ± .0659. dm = .09 ± .0912. s = 0.97.

(76) *Ambergold 1957.* 73 B of S-Aleutian-Silverblu mean 3.79 ± .0591 > 95 B of S-Aleutian-Silverblu-Ambergold mean 3.28 ± .0382. dm = .51 ± .0425. s = 12.00.

(77) *Ambergold 1957.* 19 Silverblu mean 4.26 ± .0646 > 377 Silverblu-Ambergold mean 3.76 ± .0253. dm = .50 ± .0693. s = 7.21.

(78) *Ambergold 1957.* 47 Silverblu-Aleautian mean 3.72 ± 0824 > 218 Silverblu-Aleutian-Ambergold mean 3.36 ± .0268. dm = .36 ± .0866. s = 4.16.

(79) *Ambergold Hybrids 1957.* 136 Ambergold-Aleutian mean 3.75 ± .0358 > 125 Silverblu-Aleutian (hybrid for Ambergold) mean 3.32 ± .0474. dm = .43 ± .0585. s = 7.35.

(80) *Ambergold 1955.* 158 Ambergold-Silverblu mean 2.13 ± .0205 < 157 Silverblu-Aleutian mean 2.21 ± .0298. dm = .08 ± .0298. s = 2.68.

(81) *Ambergold 1955.* 158 Ambergold-Silverblu mean 2.13 ± .0205 < 190 Silverblu (hybrid for Ambergold) mean 2.15 ± .0203. dm = .02 ± .0288. s = 0.69.

PALOMINO MALES

(82) *Palomino 1954.* 37 Palomino-Silverblu-Breath of Spring mean 3.08 ± .0332 < 184 Breath of Spring-Silverblu (carry Aleutian) mean 3.46 ± .0652. dm = .38 ± .0732. s = 5.19.

(83) *Palomino 1957.* 19 Silverblu mean 4.26 ± .0646 > 986 Silverblu-Palomino mean 3.56 ± .0204. dm = .70 ± .0325. s = 2.15.

(84) *Palomino Hybrids 1957.* 191 Silverblu mean 3.78 ± .0345 > 154 Silverblu (hybrid for Palomino) mean 3.32 ± .0424. dm = .46 ± .0546. s = 8.42.

MOYLE BUFF MALES

(85) *Moyle Buff 1954.* 25 Boyle Buff mean 4.04 ± .0164 > 56 Silverblu (hybrid for Aleutian) mean 3.35 ± .0681. dm = .69. s = 9.86.

(86) *Moyle Buff 1954.* 25 Moyle Buff mean 4.04 ± .0164 > 119 Pastel mean 3.79 ± .0511. dm = .25 ± .0536. s = 4.7.

(87) *Moyle Buff 1956.* 648 Moyle Buff mean 4.16 ± .0211 > 63 Dark (miscellaneous hybrids) mean 3.53 ± .0920. dm = .63 ± .0938. s = 6.72.

(88) *Moyle Buff 1956.* 648 Moyle Buff mean 4.16 ± .0211 > 10 Dark (wild type) mean 3.75 ± .1413. dm = .41 ± .1429. s = 2.87.

(89) *Moyle Buff 1957.* 239 Moyle Buff mean 4.43 ± .0365 > 27 Dark (wild type) mean 3.94 ± .0967. dm = .49 ± .1034. s = 4.74.

(90) *Moyle Buff 1957.* 222 Silverblu-Aleutian-Moyle Buff mean 3.88 ± .0294 > 136 Silverblu-Aleutian mean 3.75 ± .0378. dm = .13 ± .0463. s = 2.81.

MOYLE BUFF FEMALES

(91) *Moyle Buff 1954.* 48 Moyle Buff mean 2.13 ± .0412 > 49 Dark mean 1.99 ± .0272. dm = .14 ± .0494. s = 2.83.

(92) *Moyle Buff 1954.* 9 Moyle Buff mean 2.20 ± .0720 > 49 Dark mean 1.99 ± .0272. dm = .21 ± .0770. s = 2.73.

(93) *Moyle Buff 1955.* 99 Silverblu-Moyle Buff mean 2.20 ± .0283 > 196 Silverblu (hybrid for Palomino) mean 2.08 ± .0188. dm = .12 ± .0335. s = 3.58.

(94) *Moyle Buff 1956.* 64 Moyle Buff-Silverblu mean 2.15 ± .0319 < 18 Silverblu (hybrid for Moyle Buff) mean 2.15 ± .0319. dm = .12 ± .0677. s = 1.77.

HYBRID MOYLE BUFF MALES

(95) *Hybrid Moyle Buff 1954.* 49 Silverblu (hybrid for Moyle Buff) mean 3.87 ± .0804 > 56 Silverblu (hybrid for Aleutian) mean 3.35 ± .0681. dm = .52 ± .1053. s = 4.9.

(96) *Moyle Buff Hybrids 1955.* 333 Dark (wild type, carry Moyle Buff) mean 4.30 ± .0370 > 43 Dark (wild type, carry Ambergold and Silverblu) mean 3.68 ± .0745. dm = .62 ± .0745. s = 7.46.

(97) *Moyle Buff Hybrids 1955.* 65 Silverblu (hybrid for Moyle Buff) mean 4.16 ± .0649 > 154 Silverblu (hybrid for Palomino) mean 3.32 ± .0424. dm = .84 ± .0775. s = 10.85.

(98) *Moyle Buff Hybrids 1955.* 65 Silverblu (hybrid for Moyle Buff) mean 4.16 ± .0649 > 191 Silverblu (hybrid for Ambergold) mean 3.78 ± .0345. dm = .38 ± .0547. s = 6.95.

(99) *Moyle Buff Hybrids 1957.* 52 Dark (hybrid for Moyle Buff) mean 4.32 ± .0739 > 27 Dark (wild type) mean 3.94 ± .0967. dm = .38 ± .1217. s = 3.12.

(100) *Moyle Buff Hybrids 1957.* 25 Pastel (hybrid for Moyle Buff) mean 4.34 ± .0856 > 222 Pastel mean 4.17 ± .0947. dm = .17 ± .0949. s = 1.79.

(101) *Moyle Buff Hybrids 1957.* 57 Aleutian (carry Moyle Buff) mean 3.89 ± .0670 > 246 Aleutian (carry Silverblu) mean 3.71 ± .0318. dm = .18 ± .0741. s = 2.43.

(102) *Moyle Buff Hybrids 1957.* 217 Silverblu-Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 47 Silverblu-Aleutian mean 3.72 ± .0824. dm = .07 ± .0883. s = 0.79.

(103) *Moyle Buff Hybrids 1957.* 217 Silverblu-Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 136 Silverblu-Aleutian mean 3.75 ± .0358. dm = .04 ± .0475. s = 0.84.

(104) *Moyle Buff Hybrids 1957.* 217 Silverblu-Aleutian (hybrid for Moyle Buff) mean 3.79 ± .0319 > 125 Silverblu-Aleutian (hybrid for Ambergold) mean 3.32 ± .0474. dm = .47 ± .0571. s = 8.23.

(105) *Dark Moyle Buff Allel 1957.* 239 Moyle Buff mean 4.43 ± .0365 > 67 Dark Moyle Buff Allel mean 3.25 ± .0591. dm = 1.18 ± .0694. s = 17.00.

(106) *Hybrid Moyle Buff 1954.* 42 Silverblu (hybrid for Moyle Buff) mean 2.19 ± .0385 > 25 Silverblu (hybrid for Ambergold) mean 2.12 ± .0428. dm = .07 ± .0576. s = 1.21.

(107) *Hybrid Moyle Buff 1955.* 327 Dark (hybrid for Moyle Buff) mean 2.31 ± .0153 > 77 Dark (hybrid for Ambergold and Silverblu) mean 1.91 ± .0200. dm = .40 ± .0328. s = 12.19.

(108) *Hybrid Moyle Buff 1955.* 327 Dark (hybrid for Moyle Buff) mean 2.31 ± .0153 > 19 Aleutian (hybrid for Moyle Buff) mean 2.10 ± .0616. dm = .21 ± .0634. s = 3.31.

(109) *Hybrid Moyle Buff 1955.* 327 Dark (hybrid for Moyle Buff) 2.31 ± .0153 > 65 Dark (hybrid for Ambergold and Silverblu) mean 2.13 ± .0318. dm = .18 ± .0353. s = 5.10.

(110) *Hybrid Moyle Buff 1955.* 19 Aleutian (hybrid for Moyle Buff) mean 2.10 ± .0277 > 80 Aleutian (hybrid for Silverblu) mean 2.05 ± .0277. dm = .05 ± .0392. s = 1.27.

MISCELLANEOUS

(111) *Dark 1956.* 19 Dark mean 2.01 ± .0480 = 35 Miscellaneous hybrids mean 2.01 ± .0404.

SIGNIFICANT COMPARISONS REFERRED TO IN THE VECTOR MODELS

SILVERBLU

(a) Dark + Silverblu — 8.74% increase in males.
(b) Dark + Silverblu — 8.96% increase in females.
(c) Aleutian + Silverblu — 6.78% increase in males.
(d) Aleutian + Silverblu — 5.01% increase in females.
(e) Breath of Spring-Aleutian + Silverblu — 5.53% increase in females.
(f) Pastel + Silverblu — 5.97% increase in females.
(g) Ambergold + Silverblu — 5.44% increase in females.
(h) Silverblu + Aleutian — 5.52% decrease in females.

ALEUTIAN

(a) Dark + Aleutian — 4.23% decrease in males.
(b) Dark + Aleutian — 4.14% decrease in females.
(c) Silverblu-Ambergold + Aleutian — 8.78% decrease in males.
(d) Silverblu + Aleutian — 9.01% decrease in males.
(e) Silverblu-Aleutian vs. Silverblu-Ambergold — 4.93% difference in males.
(f) Breath of Spring + Aleutian — 7.45% decrease in males.
(g) Breath of Spring-Silverblu-Palomino vs. Breath of Spring-Aleutian — 4.55% difference in males.
(h) Moyle Buff + Aleutian — 5.58% decrease in size in males.

PASTEL

(a) Dark + Pastel — 9.05% increase in males.
(b) Dark + Pastel — 5.03% increase in females.
(c) Dark hybrid for Pastel vs. Pastel — 5.55% difference in females.
(d) Breath of Spring-Aleutian vs. Breath of Spring-Pastel — 6.84% difference in females.
(e) Breath of Spring-Silverblu vs. Breath of Spring-Pastel — 5.94% difference in males.

BREATH OF SPRING

(a) Pastel + Breath of Spring — 5.86% decrease in males.
(b) Aleutian + Breath of Spring — 2.88% decrease in males.
(c) Silverblu-Aleutian + Breath of Spring — 3.81% decrease in females.

AMBERGOLD

(a) Silverblu + Ambergold — 11.07% decrease in males.
(b) Silverblu-Aleutian + Ambergold — 11.57% decrease in males.
(c) Breath of Spring - Silverblu - Aleutian + Ambergold — 11.57% decrease in males.
(d) Silverblu-Aleutian + hybrid Ambergold — 10.72% decrease in males.
(e) Silverblu-Aleutian hybrid for Ambergold vs. Silverblu-Ambergold — 12.95% difference in males.

PALOMINO

(a) Silverblu + Palomino — 16.44% decrease in males.
(b) Breath of Spring-Silverblu + Palomino — 10.98% decrease in males.
(c) Silverblu + hybrid Palomino — 12.17% decrease in males.

MOYLE BUFF

(a) Dark + Moyle Buff — 13.40% increase in males.
(b) Dark + Moyle Buff — 8.79% increase in females.
(c) Silverblu + Moyle Buff — 20.60% increase in males.
(d) Silverblu + Moyle Buff — 5.77% increase in females.
(e) Dark Moyle Buff Allel vs. Moyle Buff — 6.94% difference in males.
(f) Dark + hybrid Moyle Buff — 9.64% increase in males.

(g) Silverblu + hybrid Moyle Buff — 12.52% increase in males.

(h) Dark hybrid for Ambergold and Silverblu + hybrid Moyle Buff — 16.85% increase in males.

(i) Silverblu hybrid for Ambergold vs. Silverblu hybrid for Moyle Buff — 3.30% difference in males.

(j) Dark hybrid for Ambergold and Silverblu vs. Dark hybrid for Moyle Buff — 8.45% difference in males.

(k) Silverblu hybrid for Palomino vs. Silverblu hybrid for Moyle Buff — 25.30% difference in males.

(l) Silverblu hybrid for Ambergold vs. Silverblu hybrid for Moyle Buff — 10.05% difference in males.

(m) Aleutian + Moyle Buff — 4.85% increase in males.

(n) Aleutian hybrid for Moyle Buff vs. Dark hybrid for Moyle Buff — 10.00% difference in females.

(o) Silverblu-Aleutian hybrid for Ambergold vs. Silverblu-Aleutian hybrid for Moyle Buff — 14.16% difference in males.

(p) Aleutian hybrid for Silverblu vs. Aleutian hybrid for Moyle Buff — 2.44% difference in males.

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THE GEORGIA ACADEMY OF SCIENCE

PSYCHOSOMATIC SYNTHESIS OF BEHAVIOR TRENDS IN THE TAMING OF MINK

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INTRODUCTION

A twelve year study* involving 108,717 ranch bred mink was undertaken in order to discover the factors determining domestication, because mink are in the process of being domesticated, a term that includes tameness and docility. Domestication implies the radical alteration, on a genetic basis, of that machinery the end-product of which is behavior. It is an assembling in individuals constellations of gene allels which, acting and interacting with each other, synthesize the kind of quiet, friendly behavior desired by man, in contrast to the wild and savage responses that adapt the animal for survival in the cruel and rigorous environment of the forest.

There is no doubt but that in the process of domestication there are involved the pleiotropic effects of certain coat color genes and that these gene-induced modifications include (1) direct gene-induced changes in morphology, physiology and psychosomatic behavior,[1] plus (2) the interaction effects produced by combinations of the same coat color genes.

Some of the influences of coat color genes upon body size and bodily proportions have been placed on record[2] already and the rest of the findings on the subject will be published in the near future. In the present paper we shall describe judgments of the relative tameness of several colorphase mink strains and then report upon the direction and degree of alteration in size of adrenals and gonads of the same strains as a psychosomatic explanation of the changes in behavior.

MATERIALS AND METHODS

More than 1,125 freshly pelted mink carcasses identified as to coat color were shipped from Suamico, Wisconsin, to Milledge-

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ville, Georgia, in closed metal boxes (eight or twelve carcasses to a box according to sex) in large, commercial refrigerator containers supplied with dry ice. Upon arrival, the metal boxes containing mink carcasses were stored in the local abattoir at low temperature until they could be dissected. Because the carcasses were wrapped in oil paper and the lids of the metal boxes were close fitting, evaporation was not a problem.

Most of the animals came from heterogeneous litters in which several color varieties were segregated in the same litter. All new mutants brought to the ranch for propagation were crossed with the same inbred Dark strain of mink to add vigor, after which the color varieties were mixed. This procedure made for uniformity of residual hereditary backgrounds upon which are displayed the effects of each coat color gene. Because of sexual dimorphism, only females were compared with females and males with males. Because of subtle, yearly fluctuations (weather, food, contagion, selection of breeders for size, etc.) only animals of the same annual crops were compared.

After thawing out a carcass in the laboratory, its weight was recorded and its body length and tail length were determined. Then its adrenals and gonads were dissected out as carefully as possible by the senior investigator and quickly placed in ground-neck weighing bottles to prevent evaporation. The thyroid was destroyed by the method of killing, i.e., by breaking the neck, and hence could not be studied. The glands were weighed on a Christian Becker Chainomatic balance to an estimated $\frac{0001}{A}$ gram to reduce error, although it was realized that errors of dissection are probably much greater than that order of accuracy. The skull, right femur, right tibia, and baccula were carefully cleaned and dried for skeletal proportion studies to be reported elsewhere.

A questionnaire was sent to fifty mink ranchers each having had ten years or more of experience with most of the varieties under investigation. They were asked to classify Pastel, Silverblu, Palomino, Ambergold, Aleutian and Sapphire color varieties of mink as to "nervousness" and "gentleness." These are ranchers' terms used to express "wildness and savageness" versus "tameness and disinclination to bite." Nervous mink are very active and alert. They tend to bite caretakers when the opportunity arises. Quiet mink are less active and less aggressive. Occasional gentle mink can be carried about with impunity.

RESULTS

An analysis of the returned questionnaires showed the following estimates of behavior, although some ranchers apparently paid no attention to the relative tameness of the several coat color strains:

Pastels are gentle, say 92% of 38 ranchers answering.
Silverblus are gentle, say 86% of 44 ranchers answering.
Palominos are gentle, say 79% of 28 ranchers answering.
Ambergolds are gentle, say 71% of 31 ranchers answering.
Aleutians are nervous, say 78% of 46 ranchers answering.
Sapphires are nervous, say 78% of 45 ranchers answering.

Sapphire is a combination homozygous for gentle Silverblu and also for nervous Aleutian, and hence nervousness is genetically epistatic to gentleness in Sapphires.

Black-eyed Whites are remarkable for their tame behavior. The ranch of Jim Moore was visited by both investigators one day after dark. Jim had bred Black-eyed White to Dark mink, the wild type. The Dark hybrids, with a white belly spot and white tail tip, he had back-crossed to Black-eyed White. The two-hundred-odd backcross offspring segregated in a 1:1 ratio of Black Hybrids to Black-eyed Whites. Everywhere in the animal shed Black-eyed Whites were sleeping in the cages. No Darks were observed, so the question was asked, "Where are the Darks?" The reply was that the odor of strangers had awakened them and that they were hiding in the nest boxes. The hundred-odd missing Dark Hybrid mink were found when all the nest boxes were opened, but not a single Black-eyed White that had taken refuge in the nest boxes was discovered. Jim picked up a sleeping Black-eyed White and shook it to awaken it. This animal was so gentle that it lay quietly on its back in his hands like a kitten. It was also noticed that Black-eyed Whites come out of their nest boxes about 4 p.m. and walk around calmly and fearlessly, whereas other varieties usually wait until nearly sundown before they become active.

Kohinur (Black Cross) and Blufrost were not widespread enough to be included in the questionnaire, but opinions were recorded by experienced caretakers at the Larry Moore Mink Ranch.

It is impossible to dissect out an adrenal or a gonad carefully and weigh it with great precision, then multiply by two to get the total weight of glandular material in the body, because the left adrenal and the left gonad average slightly larger than their corresponding organs on the right side, although weights of either side may be the larger. In a certain group of 122 male mink the right adrenals averaged .0319 gram and the left adrenals averaged .0361 gram. The difference of .0045 gram is 3.3 times as large as the standard error of the difference, which was .00136 gram and hence significant statistically. A group of 25 male mink showed the right testis to be 5% smaller than the left, but this difference was not statistically significant. Eighteen female mink showed the right adrenal to be 5% smaller than the left and the right ovary (before the first ovu-

lation) to be 9% smaller than the left, but these differences were not statistically significant for the small populations studied.

When for each individual the quotient of the total adrenal weight divided by body weight is compared, it is found that both male and female Dark mink have a significantly larger ratio than Pastel and Silverblu. This is in line with the majority opinion of ranchers, namely, that these two mutant strains are noticeably tamer than the Darks.

Adrenal weight in grams ÷ Body weight in grams

49 Dark males ratio	.0000904 ± .000002881
74 Pastel males ratio	.0000772 ± .000002042
difference =	.0000132 ± .000003531

s = 3.7

49 Dark males ratio	.0000904 ± .000002881
48 Silverblu males ratio	.0000739 ± .000002191
difference =	.0000165 ± .000003619

s = 4.5

48 Dark females ratio	.000100 ± .00000263
53 Pastel females ratio	.000079 ± .00000224
difference =	.000021 ± .00000345

s = 6.1

48 Dark females ratio	.000100 ± .00000263
50 Silverblu females ratio	.000074 ± .00000229
difference =	.000026 ± .00000348

s = 7.5

The smaller size of Pastel and Silverblu adrenals when divided by body weight as compared with Dark, conceivably may be due, at least in part, to heterogonic growth. It turns out from the investigators' study of relative body size that both Silverblu and Pastel mink tend to grow larger than Dark mink.

Now, if toward the end of the growth curve the rate of increase of size of adrenals and gonads is falling off more rapidly than the rate of increase in body size is leveling off, such correlations are exactly what are to be expected. If this were the whole story, then Pastel and Silverblu are tamer than Darks just because they grow to a larger size than Darks.

There is evidence elsewhere for such a point of view. Small dogs, Fox Terriers for example, are terrifically active as compared with giant dogs such as Pyrenees. Undoubtedly the Fox

Terrier acts as though it had more adrenal and gonad per unit of body weight. The present investigators have demonstrated just such heterogonic relationships in the development of various parts of the mink skeleton.

The possible effects of heterogonic growth on gland size may be investigated by comparing the adrenal weight divided by body weight and gonad weight divided by body weight for populations of ten months of age with populations of two years or more of age. The small amount of data available is instructive:

12 Old Albino male (adrenal) ratio	.0001225 ± .0000170
36 Young male (adrenal) ratio	.0001214 ± .0000220
difference =	.0000011 ± .0000

Thus adrenals of old albino males are slightly larger for their body size than are young male adrenals, but the difference is insignificant statistically.

12 Old Albino (testes) ratio	.0100	± .0024
36 Young Albino (testes) ratio	.0061	± .0005
difference =	.0039	± .0024

s = 1.6, which is not significant.

In this albino material the older animals actually increase their gland-to-body weight ratio, which is just opposite to the relationship that heterogonic growth could be called upon to explain, namely, greater tamness in Pastel and Silverblu.

The following data relates to Young versus Old Pastel females:

12 Old Pastel female (adrenal) ratio	.000079 ± .00000224
14 Young Pastel female (adrenal) ratio	.000091 ± .00000409
difference =	.000012 ± .00000466

s = 2.6, considered significant.

12 Old Pastel (ovaries) ratio	.000133 ± .0000447
14 Young Pastel (ovaries) ratio	.000189 ± .0000120
difference =	.000056 ± .0000463

s = 1.2, not statistically significant.

These data on Pastel females show a drop in gland-to-body ratio with age that for the adrenals is statistically significant, and hence heterogonic growth may be a factor with some gene mutations and not with others; or heterogonic growth may accompany one sex and not the other.

When the quotient of gonad weight divided by body weight for Pastel and Silverblu is compared with that for Dark, a significant difference is found between Dark males and both Pastel and Silverblu. Dark has more gonad per unit of body weight. With females the differences are in the same direction, being significant for Dark compared with Silverblu. However, for Dark compared with Pastel, the differences between the means of the two populations of ratios is just short of twice the standard error of the difference. This lack of significance is not surprising, considering the small size of the ovaries, and more data would probably make significant the difference observed.

49 Dark testes ratio	.007113 ± .0003915
74 Pastel testes ratio	.004616 ± .0002185
difference =	.002497 ± .0004483

s = 5.6

49 Dark testes ratio	.007113 ± .0003915
48 Silverblu testes ratio	.005317 ± .0002407
difference =	.001796 ± .0004596

s = 3.9

48 Dark ovaries ratio	.00146 ± .0000591
53 Pastel ovaries ratio	.00133 ± .0000447
difference =	.00013 ± .0000741

s = 1.7

48 Dark ovaries ratio	.00146 ± .0000591
50 Silverblu ovaries ratio	.00094 ± .0000409
difference =	.00052 ± .0000718

s = 7.2

The present findings tend, then, to explain the tamer nature of Pastel and Silverblu, in that in these two strains there is less adrenalin and less sex hormone per unit of body weight than in wild and savage Dark mink. Conceivably, such gland-body ratios may be modified by heterogonic growth as discussed above.

In order to eliminate any possible factor of heterogonic growth, matched populations of Dark, Silverblu, Pastel and Kohinur were selected from dissection data of males. Each animal in the Dark population was matched with an animal of Pastel, Silverblu and Kohinur of as nearly the same body length as possible. (Body length is a better index of growth than is weight, due to fluctuations with food obtained, elimination, temporary illness, etc.). However, for comparing the effect of

gland size on behavior, it is obvious that body weight is the best denominator for the index, due to fattening as maturity is approached, which fattening is greater in some strains than in others.

Thus, these four selected populations of gland-body weight ratios could be compared without involving any possible effects of heterogonic growth. For Blufront relatively few dissections were made, but it was possible to select animals having a spread of body lengths chosen to parallel that of the Dark population.

Using matched male populations, the comparisons of adrenal weight divided by body weight are listed below. Although animals were selected on the basis of body length, body weight was used for comparison because adrenalin strength should be proportional to the capacity of the blood system by which it is diluted.

s=0.9 { Dark male adrenals = .0913 ± .0044 grams
Kohimur male adrenals = .0871 ± .0019 grams } s=1.7 { s=2.5 } s=2.6
s=2.7 { Pastel male adrenals = .0821 ± .0013 grams
Blufrost male adrenals = .0780 ± .0030 grams
Silverblu male adrenals = .0768 ± .0032 grams }

Thus, there are significant correlations between the quotient of adrenal weight divided by Body weight ratios of Dark and Silverblu and Blufrost. The present data for Pastel are in the right direction and the significance is 1.7, approaching the value of 2 which is considered to be of proven significance.

Paired populations for gonad weight divided by Body weight yielded the following comparisons:

24 Dark male adrenals	.0765 ± .0037 grams
24 Aleutian male adrenals	.0716 ± .0037
difference =	.0049 ± .0052
24 Dark testes	.4921 ± .0336
24 Aleutian testes	.4692 ± .0215
difference =	.0229

When paired population comparisons for Aleutian females are compared, much the same results are obtained:

25 Aleutian female adrenals	.0542 ± .0021 grams
25 Dark female adrenals	.0408 ± .0070
difference =	.0023 ± .0044

Thus the Aleutians, generally agreed to be "nervous" mink when compared in paired populations with Darks for both males and females, show no statistically proven difference from the Darks in gland-to-body ratio.

CONCLUSIONS

As in previous behavior studies made by the senior author upon long-time tamed strains of laboratory rats, it is found that tameness and wildness in mink now in the process of domestication may be explained largely on the basis of adrenal and gonad size relative to body size. These gland size variations are determined as pleiotropic manifestations of simply inherited coat-color mutations. Nervousness of Aleutians is epistatic to gentleness of Silverblu when both genes are combined homozygously in Sapphires.

SUMMARY

Coat color and weight data were collected on 108,717 ranch bred mink and dissections of more than 1,125 carcasses were made. Answers to a ranchers' questionnaire are reported that attest to the natural tameness of several coat color mutant strains of mink, Pastel and Silverblu being of greatest interest. The results of the questionnaire also indicate Aleutian and Sapphire to be of a wild and savage temperament.

It was found that adrenals and gonads in tame Pastels and Silverblus are relatively smaller for the size of the body than in Darks. The relative adrenal and gonad size in wild Aleutians is not statistically different from that of the Darks.

However, because the body sizes of Pastels and Silverblus average larger than those of Dark and the body sizes of Aleutians average smaller than Darks, it was thought advisable to eliminate any possible effect of heterogonic growth that might be operating undetected in any of these strains. The possibility of heterogonic growth influence was ruled out by the method of selecting for study from the data sheets paired populations of individuals, each pair having as nearly the same body weight or body length as possible. When the possible heterogonic growth factor was eliminated, the tame Pastels and Silverblus still showed relatively smaller adrenals and gonads than the Darks. The wild Aleutians, on the contrary, showed gland-body ratios for adrenals and gonads not statistically different from those of Darks.

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XXVI

NOTE ON THE WEAKNESS OF TISSUES IN ALEUTIAN MINK

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Because Aleutian mink have become important in studies of the Chediak-Higashi syndrome that they possess, it appears worth while placing on record a brief summary of observations on the weakness of their tissues noted in 1950 while dissecting carcasses for a study of gland size, body size and behavior trends.

The pelting process in mink subjects the animal carcass to severe tension, but normal dark mink are so solidly built that the skin is usually ripped off without obvious injury to the tissues of the body.

Upon examination of a few Aleutian carcasses, however, it soon became evident, especially in females, that the tissues were frequently ripped or torn. For this reason and because blood vessel weakness and alimentary tract difficulties were already known in Aleutians, any ripping was noted on the dissection records of 326 mink of several color phases, many of them from litters segregating for several colors. A summary of these entries is shown in Table 1.

TABLE 1

Normal and ripped carcasses among several colorphases of ranch bred mink.

Colorphase	Normal Carcasses	Ripped Carcasses	Percent Ripped
Normal male	51	3*	6
'' female	49	0	0
Aleutian male	32	6*	16
'' female	56	25	31
Blue Frost male	38	4+	10
---	---	---	---
Kohinur male	16	1+	6
---	---	---	---
Albino male	27	4	13
'' female	12	2	14

*Three with one or both testes missing.
+One with a testis missing.

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The most common injury was the ripping loose of the kidneys which were sometimes thereafter found in the pelvis. Next in frequency was the ripping open of the entire body wall laterally at the level of the diaphragm. Rarely an ovary was torn loose, or the diaphragm was burst. Once an adrenal was found detached, and once a tail was yanked off. Several times an adrenal was torn in two.

If the Aleutian female percentage of 31 ripped among 81 animals is compared with the normal dark female group of 49 animals in which none was ripped, the difference in ratios is found to be significant.

In viewing Table 1, special mention should be made of loss of testes. We cannot say whether a testis adhered to the skin and was torn off or was congenitally absent. The former appears more likely.

DISCUSSION

As we go deeper into the study of genetic constitutions and their physiological relations to health of the individual, many facts previously thought to be of little importance increase in significance. For example, Blue Frost carcasses were found to be very fat, but there was little connective tissue on the adrenals. The adrenals of Kohinurs cleaned readily. Pastels and especially Silverblues were huge and very fat. All these items reflect differences in constitution.

Aleutians were small and had not grown well. This condition reminds one of other mutations in mammals known for many years. For example, Donaldson pointed out in 1915:

"When body lengths are the same: The Norway rat has a smaller body weight, a greater brain weight, a greater spinal cord weight, a higher percentage of water in the central nervous system; heavier testes, ovaries and suprarenals - - - - - - - - - .

"These differences taken together indicate that the albino rat has grown less well, and it seems most natural to attribute this lack of growth to the whole set of conditions summed up in the word domestication."

Keeler and King (1942) credited these changes to the coat color genes non-agouti, albino and hooded. Schopbach, Keeler and Greenberg (1943) attributed alterations in the basal metabolic rate as well as heart rate to mutant genes. Keeler (1946) showed that natural rates of osseo-desiccation were altered when rats possessed certain genes, and (1947) that altered temperament (affecting behavior) in certain strains of rats could be accounted for by their possession of certain coat color genes.

In 1939 my assistant, Miss Ruth Meeser, had etherized a dozen adult rats (a male and a female from six different strains) and had laid them out side by side prior to dissection. Then she asked me to feel their muscles. I did so and found the 55th generation of captive gray Norways to be solid muscled, but the mutants derived from them to be, in general, soft. The Wistar laboratory albinos (containing non-agouti, hooded and albino genes homozygously) had the flabbiest muscles of

them all, although one cannot accuse the Wistar strain at that time of being unhealthy.

The field of muscular strength and muscle tonus as related to health and pigment genes is still waiting to be explored.

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XXVII

FOX FARM VISIT

Mr. Ed Fromm stopped his pickup truck and unlocked the high, iron-framed, heavy wire gate to an enormous priming range. He stayed outside because the foxes had seen him before, but instructed me as a perfect stranger to follow the road into the forest of shady pines and "see what happens."

I did as I was advised and walked for a thousand yards under the trees to a large, iron food trough, since it was feeding time and numbers of foxes could be seen at a distance gradually moving toward the center of alimentary attraction. As I walked I soon noted that a pack of six or seven curious Amber Foxes was trailing me at about fifteen feet. Several other fellows came in from either side to escort me, trotting parallel to the road at about the same distance. Finally, two foxes beyond and to the side of the road took positions on it and marched at the head of our procession.

It was readily noticeable that the foxes were nervous because they held their tails stiffly and bushed, and some of them defected. They looked up at me distrustfully as though I was too large for their confidence. However, being foxes, they were curious and investigative and wanted to see what I was going to do.

When I arrived with my entourage of foxes at the feeding station I made myself small by getting down on one knee, and this seemed to relieve somewhat the tension of my hosts. I held my wrist to my mouth and produced a series of mousy squeaks. At this an interested crowd began to close in on me from every direction. All the foxes near me were Ambers with an occasional Glacier. Farther away I could recognize a Pearl or a Silver and in the far distance a few Platinums. Red foxes never show themselves like this, although they sometimes find their way into the range. "In fact, we never see them until the final round-up," explained Mr. Fromm.

Whereas, the nearest Ambers maintained a respectful distance of some ten feet, one daring little female came up and ate from the trough twelve inches away from my hand, but kept a wary eye upon me all the while.

The sun was setting behind me, throwing long shadows upon the ground. I could see my large, crouching, stationary shadow with three little fox shadows sneaking up behind mine.

Finally, there was a sudden, sharp jerk on my coat tail and the three foxes protesting my presence fled to safety.

My observations were: Reds are never seen on the range. Platinums and Blacks with one coat color gene mutation, remain on the horizon. Pearls with two mutant genes come closer to strangers, while Ambers with three and Glaciers with possibly four mutations combined show very little fear. This must be another case of behavior synthesis leading to tameness. We must investigate it.

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Coat Color Gene Synthesis of Tame Behavior In the Rat, Mink and Fox

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Purpose

The purpose of this paper is to show that the gene quantum is the unit of normal behavior tendency just as it is the unit of normal anatomy and normal physiology. And a good way to demonstrate the presence of an altered behavior tendency is to have it associated pleiotropically with some physical marker such as coat color in an animal, the behavior tendency and the marker both stemming from presence of the same gene in an individual. An externally visible coat color or other marker permits genetic manipulation. It becomes a label telling us what constellation of pleiotropic alterations in-physiology is present inside. Then, if we combine in a single individual animal, let us say, three monogenic coat colors, their visibly recognizable "combination- coat color" label informs us what three physiological syndromes are interacting within. If these physiological syndromes have behavior manifestations we will be able to observe in the resulting behavior of the animal the behavior synthesis derived from their interaction. If three or more coat color genes, each producing slight tameness, for example,



Clyde E. Keeler, Sc.D.

are combined in the same individual we may logically expect their effects to be additive, thus synthesizing a completely tame animal by means of pigment gene pleiotropy.

Materials and Procedure

In 1941 I was working with the coat color mutant strains derived by Dr. Helen D. King from her inbred stock of captive wild gray Norway rats. Miss Ruth Meeser pointed out to me that the black (non-agouti) derivatives tend to be tame. The striped rats are slightly more docile, but nervous. The albino mutants show very slight tameness tendencies. It should be stated that the very tame domestic Wistar albinos contain in homozygous from all three of the above mentioned genes. Upon examining the unpublished dissection records of the late Dr. H. H. Donaldson it was shown that the physical modifications possessed by black, hooded and albino monogenic mutant strains, if added together, would largely account for all the modifications of Wistar albinos as compared with Wild gray Norways.[1] These latter modifications had always been considered by investigators to be the logical psychosomatic cause of tame behavior in laboratory albino rats but nobody had associated them with coat color genes.

Work was continued on the role of pleiotropic modifications in morphology and physiology associated with coat color genes in the production of behavior. Obviously, one could try to make a tame albino into a wild gray, or one could attempt to change a wild gray into an albino and try to observe what genetic factors were involved. In the hands of a number of persons both projects had failed. I suggested that if physiological changes associated pleiotropically with coat color genes were a principal cause of alterations in the behavior of mammals rather than associated with linked genes on the same chromosome, this matter could be tested best in the mink, a savage carnivore, raised meticulously in enormous numbers and now yielding more than a dozen coat color mutations.

Because the rat and mink function on such a low level of mentality that their wildness or tameness can only be measured by such simple devices as counting the several reactions made under manual restraint for one minute, it was decided to examine the ranch bred fox, an animal operating on a

very high level of cerebration like the dog. The experimental animal could not be the dog itself, however, because the dog had been tamed for several thousand years. The fox now has half a dozen coat color mutations suitable for examination.

Methods

We have made anatomical and physiological tests on rats and mink containing single coat color mutations in order to establish the pleiotropic manifestations of these mutations. We have combined coat colors and observed the results of these combinations on behavior.

In the foxes we have made observations of relative tameness on the priming range, with reference to their coat colors.

Results

In 1942 we published Modification Profiles [2] for several strains of coat color mutants derived from the inbred captive Wild Gray Norway colony at the Wistar Institute. These mono-mutant strains were albino, chocolate, hooded, black and curly. We presented Modification Profiles for two di-mutant strains: black hooded (containing black (non-agouti) and hooded: also albino waltzer. Waltzer is a gene that modifies both bodily proportions and behavior. The elements recorded in these pleiotropic manifestations included body weight, body length, tail length, nasal length, fronto-occipital length, squamosal distance, cranial capacity, femur length, humerous length, thyroid weight, hypophysis weight, suprarenal weight, gonad weight, brain weight, paraflocculus weight, olfactory bulb weight, relative exercise, wildness, and savageness.

It was found that if the modifications due to the non-agouti gene are combined with those due to the piebald gene we obtain still greater physical and behavioristic changes such as are present in the Hatai Piebalds that contain both non-agouti (black) and hooded (piebald) homozygously.

In 1942 we made a special study of the behavior of black mutants.[3] In two holding tests, four emergence tests, and an annoyance test we found the blacks in a segregating population of 125 animals to be definitely tamer than the grays. The disturbed animals in the annoyance test were largely the same individuals disturbed in the holding test.

A garlic smelling test suggested that the albino gene dulls the sense of smell.

A comparison of basal metabolic rates [4] for segregates of various coat colors showed that our Wild grays operated at a lower rate than did the albinos, Hybrids between Wild gray and albino tended to inherit the lower rate of the wild Gray. We concluded that the most important factors in the alteration of basal metabolism was the coat color genes. We also observed that heart rate varies with coat color.

Voice analyzer records showed that animals of specific coat colors tended to have voices with distinct characteristics. We published an analysis of the voices [5, 6] of Wild Gray, albino, ruby-eyed dilute, chocolate, curly, black, and stub rats. In general the fundamental pitch of the voice is raised in mutants and the voice of the albino mutant tends to be a single frequency.

Muscle tonus is usually much less in the mutants than in the Wild grays.[7]

The length of tail was found to be decreased in the hooded mutant,[8] whereas it is elongated in the Wistar albino.

That even more subtile changes are associated with coat color genes is shown by the data assembled by Dr. Donaldson on osseo-desiccation.[9] By studying his post-humous records we found that there is a cephalo-caudadly oriented axial gradient of increased natural desiccation detectable in nine strains of rats containing single mutant genes on the Wild gray Norway background. Certain behavior alterations associated with the coat color genes were listed in the paper just cited.

We were able to demonstrate that the coat color genes have specific, associated body sizes,[10] and that these characteristic sizes are additive if one respects the plus and minus signs. Of course, there is a size limit and although two plus genes for body size will make an animal still larger than one plus gene would make it, the size is something less than the actual sum of the separate effects of the two genes. Likewise two genes for small size will make an animal still smaller. A plus coat color gene and a minus coat color gene together in the same individual make an animal of about normal size.

A detailed statistical study of the figures on which were based the pleiotropic modification charts of Keeler and King revealed [11] that most of the differences reported were statistically significant. Certain effects of individual coat-character genes are evident in the morphology, physiology, and behavior of genetically simple strains bearing one modified gene. Some of these effects appear in synthesized strains built up genetically so as to contain homozygous combinations of two and also of three each coat-character genes on the Wild gray residual hereditary background.

The behavior effects resulting from brain and gland modification produced by the genes for black and hooded and to a lesser extent albino, played a leading role in the original domestication of the laboratory albino rat, although it has probably been selected unwittingly ever since by man and the laboratory environment for other unlabeled tameness genes.

Dr. King's captive gray Norway rats never did become tame during 55 generations. At the end of this period I was well acquainted with the 55th generation of these captive Gray rats. They were still thrashing demons, shrieking and scrambling and cowering in the corners of their armored, stainless steel cages. When Dr. King wanted to catch one of these animals she would soak with ether a huge mass of cotton and throw it into the group packed into a corner of the cage, quivering and squealing with fear. When they had all passed out she would remove by the tail with tongs the desired but groggy rat and hustle it into a covered jar before it had a chance to attack her.

A general survey of mammals was made, and a list of those in which behavior alterations were said to be associated with coat colors was published.[12]

We decided that since pigment gene pleiotropy is so abundantly evident in the rat (a rodent), it should be sought in the mink (a carnivore) in order to

test its general applicability to all mammals. The easiest effect to test was size. Figures for size showed segregates for Silverblu, Breath of Spring Silverblu, Blufrost, Kohinur, all to have distinct average body sizes in both males and females.[13]

Later studies over a period of 12 years revealed that these segregates maintain their distinctive body sizes relative to each other.[14] To the coat color mutations affecting size were later added Aleutian, Pastel, Ambergold, Palomino, and Moyle Buff genes. Body proportions are definitely modified by coat color genes.[15]

A questionnaire survey of relative tameness and wildness, sent to fifty ranchers of mutation mink, each having ten or more years of experience with mutant coat color strains, revealed that animals carrying the Aleutian gene homozygously are "nervous" and ill tempered, that those bearing Pastel and Silverblue are "calm" and more docile. Adrenals and gonads in Aleutians are large for a given body weight, not statistically different from those of wild drak mink. The adrenals and gonads of Pastels and Silverblus are statistically smaller for body size than in dark mink or Aleutians.

By combining coat color genes each having a slight taming effect we are in the process of taming the mink. Because of genetic difficulties it will require several years more to entirely complete the process, although results to date assure us that it will be accomplished.

It occurred to us that we should also look for pleiotropic effects of coat color genes in some animal of high intelligence possessing more ways of expressing behavior than in rats and mink, as we mentioned at the beginning of this article. The animal voted as most suitable was the fox.



Adult male non-agouti mutant of the Norway rat caught at the Milledgeville State Hospital. The photo was taken when this rat was picked up for the first time. It is quiet and peaceful.

I visited a fur farm in Wisconsin to make a preliminary examination of mutant foxes. Seven hundred foxes were being primed on immense ranges.

At feeding time I visited one extensive priming range planted with pines in which the foxes run loose. Occasionally wild foxes manage to get onto these ranges from the outside. However, they are never seen by the caretakers until the final roundup when the range is combed by a line of 150 men who drive them into a huge spread-funnel net. At the periphery of visibility on the range I saw silvers (black mutation + multiple factor graying). Somewhat closer were a few pearls (black + multiple factor graying + pearl mutation), and platinum (black + multiple factor graying + platinum mutation). In the foreground were ambers (black + multiple factor graying + pearl + chocolate mutation). These ambers swarmed about



Colorphases of the Red Fox. The tamest are the Ambers in the foreground bearing homozygously the taming genes non-agouti, blue and chocolate.



A well behaved Silverblu mink showing no animosity or fear.

me but usually kept a respectful distance from me of 15 feet or more.

On another range, after feeding time, the silvers, platinums, pearls and blonds had disappeared beyond the periphery of visualizable area, but everywhere there were ambers lying or walking about. I counted 100 of them. I reduced my size by crouching down and made a noise like a mouse. The ambers converged from all directions, many coming within 15 feet of me and several within the distance of one yard. Three or four advanced behind me and sniffed, because I could see their shadows on the ground, and one of these sneaked up and gave my coat tail a yank. I believe that without further attention the ambers will make intelligent house pets.

These coat color combinations in the fox also have specific size tendencies as in rats and mink. Ambers, for example, are small and their fur is somewhat silky. Some of the skulls have specific shapes. Ambers have short muzzles. A study of the sizes, shapes and glandular variations is being made. It is highly probable that this synthesis of tameness in the fox is based on pleiotropic modifications of glands, sense organs and brain produced by the coat color genes, just as they were found to be in the other two species studied.

Summary

It is evident from my description of King's Gray Norway rats after 55 generations of captivity that the small-effect unidentified genes to which Richter attributed domestication in his albino- black- hooded colony had not taken them very far on the road to tameness.

However, by combining those same albino, black, and hooded mutants derived from King's wild strain I produced tame rats that possess physical "marks of domestication".

I have shown that mink exhibit typical "marks of domestication" and that taming genes with coat color manifestations exist also in mink.

My observations on mutant foxes confirm the presence of coat color mutations due to taming genes in a species living on a high level of cerebration, with many possible modes of response.

Thus, we have demonstrated the gene-quantum to be the unit of normal behavior. When a coat color and a

behavior alteration are produced by the same gene, the coat color may be used to modify behavior in a desired direction by means of the pleiotropic changes in morphology and physiology associated with the coat color. If several coat color genes, each having its own pleiotropic "marks of domestication" are added together in the same individual of a wild stock that animal will be tame.

Human applications of this work will be found in such areas as the study of albinos [30] and red heads.

Discussion

The H.H. Donaldsons went to England not long after their marriage and Henry made it his business to visit a bushy-browed, bald-headed, white-bearded old naturalist at Suffolk, Downs, by the name of Charles Darwin. The young visitor asked what studies he could undertake that would be of value to the understanding of Evolution and the old sage replied that there needed to be experiments performed on the domesticative process in mammals. Some wild species should be taken into the laboratory and watched and measured carefully over many years to see how tameness takes place together with the remarkable genetic changes in anatomy, physiology and behavior that accompany it. Donaldson never forgot the thrill of that interview nor the problem Darwin had suggested. And so, upon retirement from his chair of Neurology at the University of Chicago, he joined the Wistar Inst. spending the rest of his life in the study of domesticative alterations in the Norway rat. He sought to know how the changes in morphlogy, physiology and behavior came about, but the fact that he was a neo-Lamarckian hampered his work. He felt that pressure of the new environment carved or moulded the animal in a mysterious fashion.

I did not ask Donaldson, whom I first met in his late seventies, whether Darwin had suggested specifically that he look into how the wild and savage Gray Norway rat gave rise to the tame and docile laboratory albino. It is true that Darwin had written about all the domesticated animals recorded in the literature, and had failed to describe the taming of the rat. However, at the time of publication of the Origin of Species in 1858, there were tame albino rats in London and scientists had no idea of how they had suddenly become tame. At any rate, Donaldson brought back from England some tame laboratory albino rats that eventually became the progenitors of the famous Wistar strain, now used in so many laboratories all over the world.

A number of persons including myself have outcrossed Wistar albinos to wild gray Norway rats, and have thus learned from the second generation that the Wistar albinos are purebred for the genes for black (non-agouti) and hooded (piebald) in addition to the gene for albinism.

It is interesting to note that eleven years before the appearance of Darwin's Animals and Plants under Domestication, James Rodwell, in 1858, published the following concerning albino rats [16]: "In London, at the present time, those animals, being bred for fancy, are becoming very numerous, and sell at the rate of four shillings a couple." Rodwell continues: "The first who bred these for fancy

and profit was a person by the name of Ostin, residing in the Waterloo Road; and he was the first man who brought to perfection the happy family, which may be seen daily at the foot of Waterloo Bridge, London. He informed me that he first procured two white rats, male and female, from Normandy about three years ago; and from this couple he had bred an immense number in cages.—He had crossed the breed with the brown (gray) and black rat; and has produced a vast number of both brown and white, and black and white piebald young ones, which are pretty little creatures and as tame as kittens." Thus, Rodwell's tame albino rats, derived from Normandy and England, contained the black, hooded and albino genes just as did those that Donaldson brought from England. It is possible that Donaldson's rats were descended from Rodwell's stock. Rodwell's black hooded segregates are "as tame as kittens" just as were those that I derived from Wistar albinos crossed to wild gray Norway rats.

Richter's excellent work on "marks of domestication" in the laboratory rat,[17] was carried out on a colony containing the genes black, hooded and albino (purebred for black and hooded). On some points Richter has advanced farther than I have, but on other points I have gone beyond him and on a third group of points, especially of interpretation, I cannot agree with him at all. Some of Richter's findings should be discussed.

Richter says: "Absence of skeletal differences between the domesticated and wild rats is indicated by their almost identical relationship of body-weight to body length." One may take exception to this statement since Donaldson and I have found small units of body size, either plus or minus, are correlated with certain coat color variations in rats, and I [10] have observed this also in mink,[14] and foxes.[7] Albino Cuna Indians are smaller than their controls.[18]

That the adrenals of tame rats are smaller than those of wild gray rats was shown by Watson [19], H. H. Donalson [20], J. C. Donaldson [21] and myself [11]. Richter also found this to be true [17].

Altered organ size was studied by Donaldson, Keeler and King [2, 11] for adrenals, brain, hypophysis, gonads, thyroid, thymus. To this list Richter and his associates [22] added preputials, liver, spleen, heart, kidneys, pancreas, uterus, seminal vesicles, prostate, fungiform papillae of the tongue [23] and Peyer's patches. There is general agreement on most alterations but whether or not the thyroid is reduced is open to question.

Richter, Rogers and Hall found that adrenalectomized tame rats survived on salt therapy [24] whereas similarly treated wild rats died. He found that resistance to poisoning with thiourea is very low in the tame rat. As studied by Griffiths, the airblast threw twenty percent of wild rats into audiogenic seizeures [25] but no tame rats had seizures.

Richter [17] says that: "During the 28 years of existence of our colony the rats have become progressively more tame." Richter feels that this is simply the result of selection of the laboratory environment upon unidentified genes present within the stock. For example,

the tamest individuals genetically are the ones most likely to breed most freely and therefore leave offspring in the greatest numbers.

I agree that this is truly one of the sets of gene factors at work. But there are other categories of gene factors to be considered. There is inbreeding in every laboratory colony and inbreeding brings to the surface recessive genes. More than half of the coat color mutations with which I have had experience in rat, mink and fox are recessives, and carry a slight taming tendency with them. For this reason we may suppose that many recessive genes in the stock, but without color manifestations, do the same. Inbreeding will bring them to the surface and into natural selection of the tame environment. The other causes not considered by Richter is the list of modifications associated with the black gene, the hooded gene and the albino gene as listed by Donaldson. I have observed the effects of these three genes singly on the wild Gray Norway residual hereditary background (which stocks were not available to Richter) and by combining all three have made tame albino rats [7]. I also added the chocolate taming gene. Undoubtedly the combination of black, piebald and albino genes in Richter's tame rats contributed most of their tameness, although he did not know it, since with these three coat color genes alone, I have tamed rats. Genetic segregation and natural selection of genes without coat color labels also played a part in taming the rats studied by Richter, but Helen D. King's captive gray Norways never did become tame.

There is confusion in the literature about the state of tameness of these animals because Dr. King once stated that her captive Grays had been domesticated and now could be used as tame laboratory animals. However, this could not be done unless they were individually hand tamed each day, beginning before their eyes opened. And even then, they were tame only to the individual who had fondled them each day. To others they were almost as savage as if they had just been caught in a barn. It required two weeks for them to be accustomed to a new caretaker, and if a stranger entered the building they would hide in their nesting material.

Richter carried out extensive tests on dietary self-selection. I performed some experiments and found that rats of different coat colors differ in their choice of diet and habit of chewing on a block of wood but I did not have facilities at the time for extensive work.

The peculiar attitude of wild rats that have once tested poison and thereafter tended to sit upright (schizophrenic withdrawal?) was investigated by Richter.[27] Stress in captivity and its tendency to enlarge adrenals and thymus was also studied.

One quotation suggests that Richter has been unaware of pigment gene pleiotropy producing typical "marks of domestication." He says: "Our knowledge of the progress of these changes from the wild ancestor to the present day domestic rat is very limited. That such changes probably progressed at a gradual rate is likely from observations made by ourselves and others who have had colonies for any length of time. Over the years the rats become tamer, less fierce, less apt to bite, or to

escape - - - - King and Donaldson "found that from one generation to the next gradual changes in organ weights and behavior occurred that were all in the direction of the present day domesticated animal but at the 25th generation *only approached* the average levels of the domesticated rats."

"Selection seems to have played the most important part in the production of the differencies between these two strains. By selection we mean here not the natural selection of wild rats in their natural habitat where the wildest, fiercest and strongest—fitted for that environment—survive, but selection in the artificial environment of the laboratory where the fittest for this type of environment survive—those that are most tame, gentle and fertile." I agree to this natural selection of the laboratory environment upon unidentified, small-effect genes.

The application to man has been called attention to by Cook [28], and by myself.[29]

Richter [17] likens these changes to those that tamed our primitive ancestors. He calls attention to the reduction of modern man's adrenals, thus producing a high rate of rheumatoid arthritis, asthma and many other diseases that yield to treatment with extracts of ACTH.

Yerkes (1913) [31] reported a study on the heredity of savageness, wildness and timidity in the gray (brown) Norway rat. He tried to rate wild rats, tame rats, F_1 and F_2 hybrids on a 5-point scale. Although tabular data are not given for the wild and tame stocks crossed, he did give data for the hybrids that were checked for probability by Stone (1932) [32] and the differences claimed by Yerkes were found to be statistically satisfactory.

Of these experiments Yerkers reports: "the second generation of wide (stripe) by wild individuals grades nearly as high as the first generation and is thus in marked contrast with the second generation of narrow by wild rats." Genetically, Yerkes is actually saying that F_1 animals backcrossed to the wild P_1 are wild, savage and timid in marked contrast to the F_2 of his gray wild X black hooded tame rats.

The conclusion drawn by Yerkes is as follows: "This apparently indicates that savageness, wildness and timidity are of a lower grade development in the second generation of wide (F_1) by wild (P_1) individuals." Stone criticizes these results by saying: "Thus the foregoing conclusion, based on the means alone, is very weak if not unwarrented." To me Yerkes results are as expected, because any recessive genetic factors underlying tameness will tend to become homozygous in the F_2 but not in the F_1 X P_1 wild backcross.

It must be remembered that in addition to the three coat color genes (black, hooded, and albino) that I have shown to be taming genes, the Wistar albino had been inbred for about fifty generations at the time of Stone's experiments and hence was relatively homozygous for other unlabeled recessive taming genes occurring from time to time by mutation and selected by the laboratory environment. These should give a slight taming effect to brown (gray) quarter blood animals as shown by Stone's curves because they, as well as the coat color labeled taming genes, would tend

to become homozygous in the backcross of F_1 to Wistar or in the F_2 of the cross between wild gray Norway and Wistar albino.

Richter seems to take it for granted that the coat colors (black, hooded and albino) have nothing to do with temperament, and hence he does not study them. He refers in 1950 to the work of Stone 1932 and possibly felt that Stone had settled the matter once and for all in the direction of Richter's own thinking.

Stone says further: of Yerkes experiment, "relatively large and reliable differences are found between the F_1 wide and the F_2 narrow. Were it not for the fact that rating scores of the F_2 generation of narrow hybrids dropped so markedly from those of the F_1 stock of narrow hybrids, there would be no reliable indication that the influence of the wild blood in the wide females was manifested in the behavior of the hybirds. So far as we can see, there is no substantial reason from the standpoint of genetics for expecting such a drop in the F_2 generation. A likely supposition is that it was brought about by some extraneous, non-hereditary factor associated with the rating scheme or with the handling of this group of animals. Such a drop was not obtained in the case of the second generation of wide-striped hybrids, which, we believe, is as it should be." However, in my opinion Stone is wrong in his criticism because wide stripe animals may be heterozygous for the hooded gene whereas narrow stripe animals are likely to be homozygous for the hooded which I claim to be the taming gene.

Yerke's results are exactly what I would expect, and are excellent considering their pioneer status in the field of animal behavior.

Sadovnikova-Koltzova (1926) [33] experimented in behavior situations with the descendants of a wild male and an albino female. "It was estimated that they had obtained approximately three quarters of their chromosomes, from the wild male and F_1 male derived from this wild and albino parentage." Evidently no attention was paid to the coat color segregates or to the matings and hence this study appears unsuitable for genetic study. Since the time per trial varied wldely from about 1 minute to 2 hours, it would appear that a considerable amount of genetic segregation had taken place.

Stone carried out holding experiments with Wistar albinos, yellow hoods, half breeds, and ¼ wild. The wild grays separated sharply from the Wistar albinos and yellow hoods as would be expected. The half bloods fell in between as expected, but the ¼ blood wild fell on the same curve with the two tame laboratory strains. These results are as expected, because among the ¼ bloods, 12% will have no coat color mutations. 37% will have one mutation, 37% will have two mutations and 12% will have all three mutations: black, hooded and albino.

Stone divides the quarter bloods into albinos, blacks, hoodeds and browns (grays). In the first situation the curve of the browns separates from those of the three coat color mutants. In the second situation the separation is not so clear cut. In learning situations all types overlapped, showing that temperament may be independent of learning ability.

Stone states: *"Thus, for the quarter-breeds, there is nothing to suggest that savageness and wildness are linked* with coat color." He continues: "A more satisfactory approach to this problem might have been one in which promiscuous interbreeding of the half-breeds was permitted for the purpose of procuring an F_2 generation with differences in color." Unfortunately, this plan, genetically, would have produced a smaller proportion of animals homozygous for a coat color mutation. Actually, there would be 42% having no mutation: 42% having one mutation; 14 having two mutations; 1% having three mutations.

If we compare the number of taming genes in homozygous form theoretically present in 100 animals of Stone's quarter blood wild group with those in 100 animals of the F_2 that he proposed to test we will see that the former contains about twice as many coat color genes in homozygeous form as the latter.

Quarter blood wilds

12% X 0 = 0
37% X 1 = 37
37% X 2 = 74
12% X 3 = 36

147 taming genes in homozygous form

F_2

42% X 0 = 0
42% X 1 = 42
14% X 2 = 28
1% X 3 = 3

73 taming genes in homozygous form

If Stone carried out this planned experiment on the F_2 he would probably have confirmed his erroneous belief that coat color has nothing to do with behavior.

In the summary of this section Stone concludes with the following statement "Within the quarter-breed group the data, too few in number for any generalization, indicate that coat colors are associated with varying degrees of wildness and savageness, rather than that there is a genetic linkage of the factors underlying hair pigment and these temperamental traits."

Farris and Yeakel begin their 1945 paper [34] with these words: "The domestication of gray Norway rats through more than 55 generations by Dr. Helen Dean King has not changed fundamentally. Their feral nature which as demonstrated by Keeler and King, is associated with coat color genes."

These authors continue: "Over half of the gray Norway rats defecated and urinated frequently in the same situation that elicited little or no response from almost half of the albinos. We therefore conclude that the gray Norway stain may be termed emotional, or better, fearful. Nevertheless, no clear-cut difference in behavior and temperament of the two strains was demonstrated. Somewhat the same conclusions were reached by Keeler, who investigated the temperament of black and black-hooded and gray-hooded animals, belonging to the F_2 generation following the cross of an inbred gray Norway and Wistar albino rat. Keeler contended that the black gene rendered an animal tame, but remarked that his tests did not separate

sharply the animals of the two colors. When, however, he considerel only those reactions which, in his estimation, denoted rage—ie, biting, attacking, laying ears back, snorting, and urinating—the difference between the two types of hybrids became clearer. Our results confirm Keeler's conclusions in that the gray-coated Norway, which are homozygous for agouti, and the Wistar white-coated animals, which are homozygous for black, differed markedly in savageness."

In 1942 when I first had proof that black is a taming gene, I wrote to various investigators to ask what was their experience in this respect.

Dr. Long of the Long-Evans team replied that all their animals had been handled from a very early age on and hence any possible inherent differences had been largely eliminated by handling. Dr. Castle stated that his blacks, that arose by mutation in Dr. King's captive gray wild Norway rats were "well behaved" and that only one had ever bitten him. Probably this stock contained no other taming genes aside from the black gene. Dr. Stone saw no differences between his rats of different coat colors. From Dr. Tryon I received no reply. Dr. Lashley, before answering my letter, went to his rat room to ask the caretaker and found to his surprise that there were then only blacks in his cages of mixed bloods. His caretaker explained that since the blacks were tamer than the others he had bred the blacks only, so that the stock no longer contained any gray animals.

It would appear that the results obtained by Donaldson, as well as Richter and associates do not contradict our findings, where as those of Yerkes and Stone unwittingly and those of Farris and Yeakel knowingly tend to confirm them, namely, that certain coat color genes produce pleiotropically modifications of glands and sense organs resulting in "marks of domestication on the physical, physiological and behavioristic levels. Our work shows that these effects are additive when several coat color genes are combined in the same individual and will produce completely tame animals when derived from wild stocks.

Addendum

Rosen [35] in studying timidity and aggressiveness in the Norway rat reports: "First, the findings relating to timidity confirm those reported earlier by Keeler. He reported a mean of 54 seconds for albino rats and a mean of 48 seconds for black hooded rats on a refined emergence—from—cage test. Secondly, recently completed research by the author (unpublished data of Rosen) has shown that the black hooded rats are significantly more dominant in competitive feeding situations than the albino rats."

Becker [36] who trapped 146 black mutants of the Norway rat in Greater Berlin during 1948-1950, has the following to say: "According to these considerations it must appear surprising that actually no more than 1.8% on the average of all migratory rats (Rattus norvegicus) in Berlin are black. From this fact one may be led to the conclusion to ascribe to the homozygotic black animals a smaller value of selection than wild colored individuals have. Actually Keeler could show in laboratory tests that black migratory rats possess a con-

siderably more expressed grade of tameness compared with wild colored Individuals. We believe that we see this conclusion confirmed with blacks caught in the wild which are kept in captivity in that such animals show themselves much less nasty tempered than is customary with brown (gray) migratory rats that are deprived of freedom. Also the activity rythm of black migratory rats seems according to the evidence differently constructed from that of the wild colored ones. Thus, we could observe the black ones frequently active in the daytime not only in their cages, but could see twice an individual running around in the open in bright sunshine. (A detailed examination of these conditions is in preparation.) Keeler and King point out that black coloring is accompanied by "marks of domestication" which also can influence the pressure of selection."

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XXIX

PSYCHOSOMATICS OF FEAR IN FOXES

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EDWARD FROMM
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Fear is recognized as a very important factor in the makeup of schizophrenia and other mental disorders, and fear is one of the most outstanding instincts of wild animals. During wartime whole populations are paralyzed by fear, and individual soldiers are so "shellshocked" by fear, that they are incapacitated for life. For these reasons, an analysis of the causes of fear in animals is a research goal that may have far-reaching implications. Both hereditary and environmental factors are recognized.

During more than forty years the senior author has been interested in the hereditary psychosomatics of behavior in mammals (1), more than half of that time being devoted to studies of wildness versus tameness in the Norway rat, *Rattus norvegicus* (2), and the ranchbred mink, *Mustela vison* (7). In both rat and mink fear is abundantly evident where it appears as the crisis-producing factor that forces a response by attack or by flight. The extreme effort to get away from a fearful situation is called wildness; the response by attack is known as savageness.

The uniqueness of our studies on rat and mink is found in the fact that certain variations of the glands, sense organs and brain (5) are highly correlated in inheritance with certain coat color genes, and hence behavioral traits could be more easily manipulated in crosses. For example, combining certain coat color genes in single individuals tended to bring together genetic factors for behavior as well and hence to produce animals both physically modified (3) and tamer. Because, to our knowledge, no crossovers have ever been found between coat color and behavior tendency in the many species in which such correlations have been observed, this association has been interpreted as due to pigment-gene pleiotropy rather than to linkage. Using this method it was possible by combining three coat color mutations occuring in a wild gray strain of the Norway rat, a rodent, to produce at once a completely tame strain of laboratory animals (4). Abundant evidence was also found in the mink, a carnivore, for correlation between coat color and morphology (6), physiology (8) and behavior (9).

In order to learn whether similar correlations are present also in animals having a higher level of intelligence, the present authors undertook a preliminary survey of the situation in the

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Red Fox, *Vulpes fulva*, and several of its coat color mutations. The Red Fox is a skittish bundle of jangled nerves, and fear is its dominant instinct. Experience has shown that the early Black (non-agouti) mutant of the Red fox is definitely a tamer animal than the Red. Such forms as Silver, Platinum, Pearl, Chocolate, Glacier and Amber have been derived from non-agouti stock. The adding of the Platinum gene or the Pearl gene to the Black (non-agouti) produces animals that tend to exhibit less fear than the Black or its Silver derivative selected for white hairs due to multiple factors. The Glacier (white), produced by adding Pearl, Chocolate and Blond genes to Black, seems to presage a still less fearful animal. The tamest fox, however, is the Amber that on large, wooded priming ranges will crowd around even strangers, exhibiting great curiosity and very little fear. See Plate A.



PLATE A. Colorphase Foxes showing little fear. Animals in the foreground are Ambers.

If the genetic factors responsible for change from fearful Red fox to fearless types are highly correlated with coat color genes, such as one finds in the rat and the mink, a comparison of sense organs and glands of various types of foxes may possibly reveal the psychosomatic alterations responsible.

METHODS

In this preliminary survey we compared the Lamina cribriformis of the Amber colorphase with that of the Red. For this comparison we sawed away the cranium in order to expose the cribriform plates of six Ambers and six Reds. Because the plates are cupped forward one cannot take a single photograph that will be perpendicular to all the nerve openings in the plate. For this reason a lateral view and a view of the inferior surface were photographed at the same distance, at the same angles and with the same bellows extension for each Amber and its paired Red control. See Plate B.

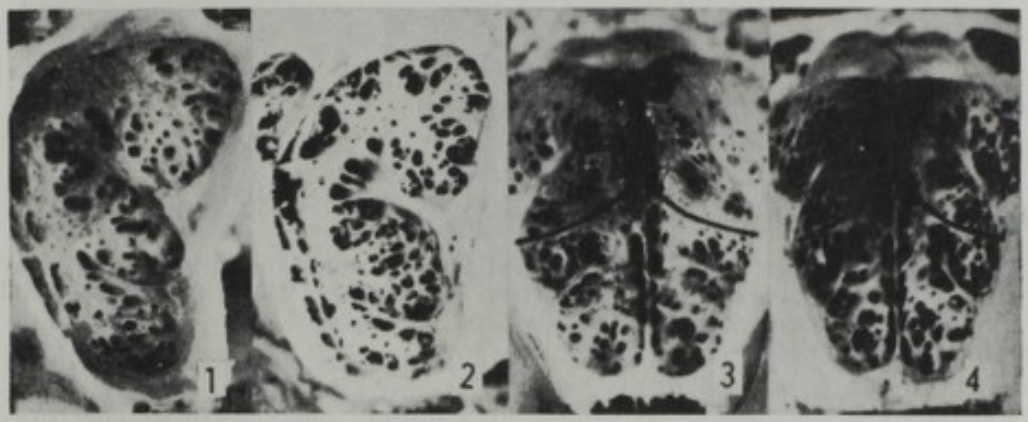


PLATE B. Photographs of cribriform plates. 1 and 2: Lateral surfaces of Amber and Red foxes, respectively. 3 and 4: Inferior surfaces of Amber and Red foxes, respectively. Area below the black line used for comparison because it is most perpendicular to the photographic angle.

These sharp photographs as taken were about one inch high. Prints from the negatives were blown up to eight or nine inches in height. A sheet of transparent plastic was stapled over each blow-up, and outlines of the nerve aperatures were drawn with India ink on the plastic. The plastic sheets were removed and outlines of the nerve aperatures, that were of many shapes and sizes, were filled in with an opaque black paint. The plastic sheets with their black spots representing nerve aperatures in the cribriform plate were placed over white cardboard and photographed with like reduction to a size that could be run through a Beckman Analytrol for scanning. See Plate C.

RESULTS

The Analytrol computations are shown in Table 1. Here it will be seen that the neural development of the cribriform plate of the Amber is uniformly reduced in development on both lateral and inferior surfaces and that we can say that Amber foxes have about 88.7% of the development of olfactory nerves compared with that of Red foxes taken as 100%. Thus, the Amber fox is



PLATE C. Tracings of the Lamina cribriformis aperatures. 1 and 4: Inferior and lateral surfaces, respectively, of an Amber fox. 2 and 3: Inferior and lateral surfaces, respectively of a Red fox.

defective in the sense of smell, and hence less aware of the dangers in its environment. It is little wonder that the Amber comes up close to sniff at human beings, especially since its fear is also reduced, probably due to adrenal deficiency, as we shall see.

A single carcass each of Amber, Glacier, Silver, Platinum and Pearl was dissected for a comparison of adrenal gland size. Five Red foxes were employed as controls. In Table 2 the gland weight in grams has been used to calculate adrenal weight in grams per 1000 grams of body weight. It will be seen that actually the Amber had the smallest weight of adrenal per unit of body weight, and that the other Colorphases were intermediate between Amber and Red. The average Colorphase adrenals were 61.1% of Red size per unit of body weight. Even if Colorphases, and especially Ambers, do sense something unusual in their environment, they should not react as violently to it as do the Reds.

In a similar fashion we compared the size of pituitary glands per unit of body weight in Colorphase foxes with that in Red foxes. These comparisons are shown in Table 3. Here it will be seen that Colorphase pituitaries average 63.6% of normal size per unit of body weight when compared with the Red ratio taken as 100%. Although the growth hormone, presumably, has made the Colorphase foxes larger than Red foxes, the relatively smaller pituitary suggests a reduction in other secretory functions, probably affecting the glandular balance of the organism.

DISCUSSION

Previous work on rats revealed that a number of genes for coat color were highly correlated with physical modifications such as the underdevelopment of glands, sense organs and brain. These alterations result in impaired physiology. For example, underdeveloped sense organs may reduce the ability to acquire accurate information about the surroundings, or the reduction in amount of adrenalin secreted may limit the response to some particular stimuli. Sense organ deficiencies make the individual somewhat ignorant of the dangers in its environment. Reduced size of thyroid causes it to operate at a more leisurely rate. Reduced interstitial tissue renders it less aggressive. Reduced adrenomedullary regions prevent violent responses when dangerous situations are sensed. Similar mechanisms were discovered in mink, and the reduction of adrenal gland tissue by certain genes correlated with coat color was shown to be directly proportional to the amount of tameness judged to be present in those particular Colorphases.

The weight of adrenal gland per 1000 grams of body weight was .144 grams in Red foxes. It was .088 for a Pearl that contains the mutations Black and Blue. It was .060 for an Amber that contains non-agouti, Blue and Chocolate. This suggests, although the present data are too few for statistical analysis, that the gland-reducing effects of the genes with which we are dealing are additive, as was the case with rats and mink.

The reduction of size of the pituitary per unit of body weight suggests glandular unbalance, possibly producing a weakening of bodily adjustments, although growth hormone may be actually increased, since the Colorphase mutants of the fox tend to be larger than the Red fox. Ranchbred foxes have been selected for size and huskiness.

Sufficient data should be collected to check these conclusions statistically, and to rule out possible alterations due to age and experience.

SUMMARY

A preliminary survey of relatively less disturbed Colorphase foxes, as compared with the fear-ridden Red fox, reveals that the Ambers have, on the average, aperature cross sections of the Lamina cribriformis reduced to 88.7% compared with those of the Red fox taken as 100%, although the cribriform plate area itself averages larger in Ambers than in Reds. Colorphase adrenals are reduced to 61.1% below the average adrenal wt/body wt ratio for Red foxes, with Amber having the greatest reduction which is correlated with the least degree of fear. Colorphase pituitaries are reduced to 63.6% of normal size per unit of body weight found in Red foxes, suggesting an alteration of glandular balance.

These findings are in keeping with previous studies of the senior author on rats and mink. They show that more intelligent animals such as foxes may be tamed by the summation of certain mutations having psychosomatic effects, when a number of such genes, each producing slight tameness, is introduced into the same individual. The strong genetic correlation between tameness and coat color is of great value to the breeder in selecting for tameness.

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Table 1.

COMPARISON OF APERATURE AREAS IN LAMINA CRIBRIFORMIS

Amber Fox Number	Red Control Number	Lateral Surface Cribriform Plate			Inferior Surface Cribriform Plate		
		Amber	Control	%	Amber	Control	%
#14	#78	24.0	25	96.0	20	24.5	81.6
# 7	#79	25.0	29	86.2	27	27.0	100.0
#20	#80	23.0	28	82.1	22	25.5	86.3
#15	#81	23.5	26	90.0	19	20.0	95.0
#16	#82	21.0	24	87.5	19	22.0	86.4
#11	#83	27.0	30	90.0	25	30.0	83.3
		Average =		88.6%	Average =		88.8%

Table 2.

ADRENAL WEIGHT IN GRAMS PER 1000 GRAMS OF BODY WEIGHT

Number	Colorphase	Adrenal wt (g) per 1000 g body wt.	Red Control Number	Adrenal wt (g) per 1000 g body wt.
#72	Amber	.060	#78	.156
#73	Glacier	.111	#79	.145
#75	Silver	.069	#80	.150
#76	Platinum	.111	#81	.134
#77	Pearl	.088	#82	.135
	Average =	.088/1000		Average = .144/1000

Table 3.

PITUITARY WEIGHT IN GRAMS PER 1000 GRAMS OF BODY WEIGHT

Number	Colorphase	Pituitary wt (g) per 1000 g body wt	Red Control Number	Pituitary wt (g) per 1000 g body wt
#72	Amber	.006	#78	.012
#73	Glacier	.011	#79	.011
#76	Platinum	.009	#80	.008
#77	Pearl	.003	#81	.012
			#82	.013
			#83	.010
		Average = .007/1000		Average = .011/1000

XXX

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GENES, DRUGS AND BEHAVIOR IN FOXES

Clyde Keeler and Edward Fromm*

IN 1942 the senior author published in the *Journal of Heredity*[3] an investigation into the association of the non-agouti (black) gene with tameness in the Norway rat, later confirmed by Farris and Yeakel[2] and also by Becker[1] and Rosen[9]. During the same year a study was published examining the multiple effects of three coat-color genes in the Norway rat making for changes in temperament, as well as their involvement in domestication[4].

Subsequently, it was shown by a number of studies that the pleiotropic phenomenon of pigment gene modification of glands, sense organs and brain[5] determining alterations within the normal range of behavior applies not only to a number of genes in the rat but also to ranch-bred mink[6] and to man[7].

Having found that progressive steps toward tame behavior could be synthesized in the rat (a rodent) and the mink (a carnivore) by adding together specific taming genes, it was decided to examine a species operating on a higher level of cerebration, namely, the red fox, *Vulpes fulva*. And because the red fox is such a

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"schizophrenic" by nature this research must also involve the use of psychomimetic drugs.

The fox will be of considerable interest to mental hospitals as a research animal for testing neurotropic drugs because the majority of their patients are schizophrenics.

In 1964 Keeler *et al.*[8] described the relatively tame behavior of color-phase foxes on large priming ranges, ranked them in fear according to the gene combinations that they possessed, and offered a partial explanation for their underdeveloped sense of olfaction, pituitary and especially adrenals. Since that report, the adrenals of 179 amber color-phase foxes (homozygous for black, pearl and chocolate genes) were dissected out carefully and weighed on a Mettler balance. The results confirm with statistical significance the reduction of adrenal weight in amber foxes per unit of body weight as compared with that for the normal red fox.

A pair of red foxes raised from before weaning to nine months of age and treated in interrupted series with Mellaril, served as controls on the behavior of a pair of ambers examined at five months of age and for 74 days thereafter and treated in interrupted series.

The most outstanding difference in behavior between the red fox taken directly from the wild and the ranch-bred amber is the enormous reduction in quantity of 1) activity and 2) fear.

Even after nine months of being with the reds twice a day at feeding time, and having tamed them to the extent that they would momentarily jump up on the experimenter's knee to take a piece of kidney from his hand, if a stranger came within thirty feet of the cage (though unseen and unheard) they would dash into their den and hide, crouching in a corner and freezing with fear.

In contrast, the pair of ambers five months old and never handled before, permitted two strangers inside their cage within eight feet of them after one week when photos were taken. On the third day that we had the ambers it was possible for one person in the cage with them to get the female, treated with Tofranil and Mellaril, to stand up on her hind legs and beg for a piece of beef kidney. The male was much more "schizophrenic" than the female and when not under medication always sought refuge in a little doghouse within the experimental cage.

The purpose of the present note is to describe and illustrate the emotional manifestations of the amber fox with and without medication.

In comparison with our wild red foxes, we can detail the behavior of our experimental pair of ambers as follows: 1) Are relatively odorless or employ their musk glands very little; 2) Have greatly reduced activity, but run in an arc on side of the wall like reds; 3) Have reduced sense of smell, but are investigative; 4) Are not so much disturbed by noises or movements in the environment as are reds; 5) Have not been heard to bark; 6) Seldom hiss or bite, tail less-often highly bushed; 7) Are not much disturbed by colors such as white (reds prefer black, fear white); 8) Do not fight back or try to bite when properly handled; 9) Retain marked "schizophrenic" fear manifested in low crouching or arched stance with ears drooped and catatonic immobility; 10) Have depressed mood in captivity. Lack affection like reds; 11) May exhibit "guilt" reaction, i.e., shifting of eyes nervously from one object to another, like a dog being scolded for chasing chickens; 12) Remain at a respectful distance of 4 to 6 feet from observer and move about in arcs at this distance constantly regarding the observer with distrustful eyes; 13) Such ataractics as Mellaril reduce fear in these foxes without affecting activity, if given in appropriate doses; 14) Such mood elevators as Tofranil and Elavil change crouching to sitting position and eliminate the eye-shifting "guilt" reaction. Cortone appears to confer a feeling of well being on them; 15) The relative degree of nervousness in both reds and ambers is indicated by frequency of urination and defecation.

Some of the responses in ambers are illustrated in Figure 8; left column under treatment, right column without treat-



TRANQUILIZED AND UNTREATED AMBER FOXES

Figure 8

Moods of the triple homozygote, amber. Left column with tranquilizers, right column, untreated. For detailed explanation see text.

ment. (*A*) Composed male, quiet but observing. The position of the ears is normal and the "squint" eyes show relaxed examination. The bodily attitudes indicate quietness and repose. (*B*) Sitting male, with the slightly erect ears of the "alert" position and "suspicious" eyes. The female is reclining and is composed. Her eyes are in observant repose. (*C*) Female, alert and begging with confidence. (*D*) Male, apprehensive; his muscles are tense and he is ready to run should the situation become more alarming. (*E*) The male will eat only in the shelter of the dog house; he keeps his eyes on the camera "distrustfully". The female is agile and is stealing food from the male. (*F*) The less schizophrenic female is stealing food from the male who shows overpowering fear that has thrown him into a catatonic state. His arched back, flexed hind legs, "droop" ears, blankly staring eyes and "tail under" attitude is typical of an extremely fearful animal. The female of both the wild red fox and the triple recessive amber derived from it is less "schizophrenic" than the male.

In the states illustrated it will be noted that 1) bodily posture, 2) bushiness of tail, and 3) appearance of the eyes and ears are diagnostic of these types of behavior.

Summary

A number of criteria diagnostic of behavior states may be recognized in the red fox and its triple mutant gene derivative colorphase, amber. These signs include position of the ears, appearance of the eyes, and carriage of the body. The chief difference between reds and amber behavior seems to be in quantity of activity and fear, to some extent dependent on the size of the adrenal glands. Personality traits such as investigativeness, lack of affection, desire not to be touched, tendency to run on the sides of a wall, remain much the same in red and amber. Depressed mood and fear in the red fox and its mutant derivatives may be ameliorated by psychomimetic medication.

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XXXI

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SUMMARY

From the comparisons described it would appear that the foxes studied can be arranged in order of their adrenal weight relative to body weight, in descending order as follows:

Wild red (no mutant genes)

Silver (black mutation and silver modifiers)

Pearl (black and blue mutations)

Amber (black, blue and chocolate mutations)

Glacier (black, blue, chocolate and white mutations)

It would appear that adrenal size reduction is correlated with both the number of coat color mutations possessed and with reduction in activity and wildness, much as we have described for mink and rats.

It would seem also that relative pituitary size may tend to decrease with addition of the coat color mutations. A similar but statistically significant reduction of the pituitary was described in rats.

The work of Levine and Christian would suggest that possibly the problem is even more complicated than we have indicated and may involve a tendency to nervously determined hypertrophy of the adrenals in animals under great stress from their environment.

If this be true, then the size of adrenal is influenced in development both by pleiotropic manifestations of the coat color genes, multiple genetic modifiers and also according to the frustrations and resultant flight activity that the individual has undergone. How extensive this effect of experience may be, we do not know, but Christian showed that it could be as great as 9% in mice, whereas the coat color gene effects on the adrenal wt/body ratio may reduce it as much as 72%.

A total of 374 foxes were dissected in this investigation.

XXXII

PIGMENT VARIATIONS AND THEIR CORRELATES IN BIRDS

BY FANNY LEE AND CLYDE E. KEELER

IN 1941 it was suggested by Keeler and King that certain coat pigmentation genes, in addition to determining melanic variations, produce multiple effects upon morphology, physiology, and behavior in the Norway rat, *Rattus norvegicus*. These conclusions were reached in view of behavior observations upon a captive gray strain of Norway rats and its several mutant—derivative strains, together with an examination of the late Dr. Donaldson's voluminous data on dissection of these same groups of rats. In 1942, Keeler published a detailed comparison of temperament in black (non-agouti) rats and their siblings bearing the gray coat color characteristic of wild Norway rats. The black mutants were found to be tamer than the grays by nature. More recent papers, Keeler (1947) have shown that this phenomenon occurs in numerous species of mammals.

An attempt to apply these findings to birds has yielded several conclusive cases. A study was made by Keeler, Hoffman, and Shearer (1949) upon many specimens of the faded-feather mutation in the Turkey, *Meleagris gallopavo*, and the faded mutants were found to have defective vision, broken or missing feathers, weak bones, and small body size.

A white, blue-eyed, mutant *Rhea americana* (about 6 weeks old) at the Philadelphia Zoo was found to be tame and unafraid of strangers as compared with its timid and excitable brown relatives.

Keeler (unpublished) has compared a pair of albino Collared Doves, *Streptopelia roseogrisea*, with a pair bearing the normal bisque coloration. The albinos have reduced ocular pigment and defective vision. They do not fly well. Their voices are relatively weak, and they are less active than the normals. After two weeks it was possible to hold the albinos on a finger, but the bisque doves would not perch on a finger even after an acquaintance of more than six months. A letter from Finn Salomonsen says that at the Copenhagen Zoo, where both varieties have been kept for many years, the albinos are less active and have weaker voices than the bisque variety.

Word from Dr. Y. Yamashina of Japan indicates that the albino Rice-bird, *Munia*, or more properly, *Lonchura*, has brownish eyes, is less active, and has a weaker voice than normally colored Rice-birds.

Because the above cases are so suggestive, it was decided that a survey of the literature ought to be made to learn whether or not other cases of pigment correlation have been recorded.

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Realizing the enormity of the task of combing world ornithological literature, it was decided to limit the survey, with two exceptions, to English language articles that could be located in the libraries of Chicago. Thus, this study is merely a sample of the literature and is, therefore, incomplete. Strong's 'Bibliography of Birds' (1936–1946) was used as the source of the references.

The descriptions of mutant birds in this restricted literature turn out to be extremely unfortunate for our purposes in that most of them were written from observations made upon dead birds or their stuffed skins, and the behavior of most individuals was not noted. Often eye-color was not recorded, and there is much confusion between piebalds and complete albinism. For this reason an accurate classification of the references is impossible, but the most satisfactory categories seem to be: (1) pink-eyed albinism; (2) "pure" albinism (which undoubtedly includes many piebalds); (3) "pale"; (4) white spotted; (5) "mottled" in several shades; and (6) miscellaneous. The results of this survey of literature have been classified according to these categories in Table 1.

In Table 1 it will be noted that the 172 recorded pigment variations have no predilection for particular orders of birds but are scattered from the lowest to the highest in evolutionary development. It will also be observed that in those groups such as the Anatidae, Phasianidae, Columbidae, Corvidae, Icteridae, Fringillidae, Turdidae, and others, mutations have been recorded that fall into most of the categories that we have employed.

Again, it should be pointed out that these types of mutations appear in general to correspond to those most commonly found in mammals, namely, true pink-eyed albinism, dilutions (especially similar to pink-eyed buff), and various types of piebald. Less common in mammals are the other types of coat color mutation which would correspond to "miscellaneous" of our classification. In Table 1 these cases are seen to be rare.

In the literature one encounters in a few cases casual mention of the correlated characteristics of individual mutants. Unfortunately, the mutants were usually shot, and hence behavior observations over a period of time were not made.

Of these cases, seven ought to be noted. The details of these mutants are given in Table 2.

No matter how deficient they may be, these observations suggest that some of the mutants of ornithological literature exhibit morphological, physiological, and behavioristic changes quite in line with those found in mutant mammals and birds following extended observa-

TABLE I

RECORDED INSTANCES OF PLUMAGE MUTATIONS IN BIRDS

Miscellaneous	*Mottled*	*White-spotted*	*"Pale"*	*"Pure" albino*	*Pink-eyed albinism*	Family of bird involved
		1				Gaviidae (Loons)
1	1					Laridae (Gulls, Terns)
				1		Sulidae (Gannets)
	2	1				Phalacrocoracidae (Cormorants)
	1	†4†	4	3	1*	Anatidae (Ducks, etc.), † = 2 mutants, * = 5 mutants)
1				1		Gruidae (Cranes)
		1	1			Rallidae (Rails, Coots)
	1	1	3	1		Scolopacidae (Snipes, etc.)
		1				Charadriidae (Plovers), Aphrizidae (Surf birds)
		1†				Haematopodidae (Oyster catchers) († = 2 mutants)
	1		1			Tetraonidae (Grouse)
	1					Meleagridae (Turkeys)
	2	1	3†	3		Phasianidae (Pheasants) († = 2 mutants)
	†2*	2		2		Columbidae (Pigeons) († = 5 mutants, * = 12 mutants)
	1			2		Cathartidae (New World Vultures)
	1			3		Buteonidae (Hawks)
		1	2			Falconidae (Falcons)
	1	1				Strigidae (true owls)
1						Psittacidae (Parrots)
1			2			Picidae (Woodpeckers)
2				1		Trochilidae (Hummingbirds)
				1		Tyrannidae (Tyrant flycatchers)
				2		Alaudidae (Larks)
	2	4	7	5†	1	Corvidae (Crows) († = 2 mutants)
		1	3		1	Sturnidae (Starlings)
	††9*‡	5*	1	1	2†	Icteridae (Blackbirds, Orioles) († = 4 mutants, * = 40% of flock, †† = 4 mutants, s = several mutants)
4*	5	†12†	3	2†	2†	Fringillidae (Finches) († = 2 mutants, * = 3 mutants)
	1		1	1*	2	Hirundinidae (Swallows) (s = several mutants)
	1					Vireonidae (Vireos)
1		2		1	1	Mniotiltidae (Warblers)
1				1		Motacillidae (Wagtails)
	2					Mimidae (Mimic thrushes)
		2	1			Troglodytidae (Wrens)
1		1†				Paridae (Titmice) († = 2 mutants)
			1			Sylviidae (Kinglets and Gnatcatchers)
1	†3††	2	2		1	Turdidae (Thrushes) († = 2 mutants, †† = 3 mutants)
14	37	44	35	31	11	SUBTOTALS
					172	TOTAL

tions. The birds may be noticeably large or small; they may be wilder or tamer than normal; they may have reduced vocal powers.

In the literature there are several references that merit special consideration.

Darwin (1890) described a physiological correlation between feather coloring and degree of development of down at hatching in pigeons. He says: "Mr. Tegetmeier has informed me of a curious and inexplicable case of correlation, namely, that young pigeons of all breeds which when mature become white, yellow, silver (i. e., extremely pale blue), or dun colored, are born almost naked; whereas pigeons of other colours are born well clothed with down."

TABLE 2

Bird	*Color*	*Morphology, physiology, behavior,*
Coot (*Oidemia* sp. ?)	dirty white; underparts of wings bleached brown; eyes black	head of flock
Vulture (*Cathartes* sp.)	white	small, but leader of flock
Hawk (*Buteo* sp.)	partial albino	showed fear of other hawks
Red-tailed Hawk (*Buteo i. borealis*)	albino	extra large and robust; 25 years old
Swamp Sparrow (*Melospiza georgiana*)	male; white except one dark feather	very fat; very shy
Blue Titmouse (*Parus caeruleus*)	head, neck, wings, and tail French gray; under parts canary yellow; eyes pink	size small; semi-tame
Thrush (species ?)	red breast	wilder bird; more reserved vocal powers

Maw (1935) detected in chickens what may turn out to be larger body size associated with silver feather color or slow feathering, the genes for which two characters reside on the sex chromosome. The differences were not considered statistically significant, and because the silver feather color and slow feathering genes entered the cross on the same chromosome, it was concluded that there also resides on the same chromosome a gene for large body size. But because the silver color gene and the slow feathering genes were not separated and studied further, it is impossible to say whether the size effect noted was due to a linked gene or was a pleiotropic effect of either the silver color gene or the slow feathering gene.

After 18 years in captivity a strain of Mallard Ducks described by Hunter (1939) produced a light-feathered, generally-recessive mutation. Light Mallards were interbred. Of 42 eggs set: four were infertile; seven died too early to determine feather color; 27 light Mallards died between the 23rd day and hatching time; four light

Mallards hatched but died within a few days. It would appear that a semi-lethal weakness of embryo and duckling is associated with the light gene. A back-cross was made of (Light Mallard by Fawn Indian Runner) by Light Mallard. A total of 59 eggs were set: eight were infertile; seven died too early to determine color; 24 of Normal Mallard color and 15 of Light Mallard color died between the 23rd day and hatching time; two Normals and three Light Mallards hatched and died within a few days. As compared with this high mortality among ducks bearing the Light gene in simplex or duplex, a cross of Light Mallard to Fawn Indian Runner is instructive. Twenty-nine eggs were set: three were infertile; five died too early to determine the color; ten Blue-gray blends died between the 23rd day and hatching time; ten Blue-gray blends and one Light Mallard were hatched.

These experiments were not carried far enough to decide whether the semi-lethal effect is due to the Light gene itself or to another gene linked on the same chromosome.

Probably the most satisfactory case in the literature, in which mutations among wild birds have been observed, is that reported by McIlhenny (1940). This observer watched 12 nests of Mockingbirds—all belonging to a male and his two successive mates. The male and his first mate were apparently heterozygous for albinism. Of their 43 offspring hatched, 18 were albinos and 25 were normal. "The albinos were deficient in sight, weak in voice, and not as active on the wing as their normal nest-mates. All normal young except two survived. No albinos survived."

But lest the reader should get the idea that all pigment variations are associated with weakness we should mention the description of Hachisuka's dark mutant pheasant (Legendre '1941): "The bird is large and robust. As a game bird, the Dark Pheasant presents itself as flying high and fast. Its weight is greater than that of ordinary pheasants."

Although the specific physical, physiological, and behavioristic defects of mutant birds are seldom recorded, ornithologists have a definite feeling about the matter that is well summed up in a series of articles by Legendre (1935):

"In nature, cases of albinism are often observed and collections contain numerous specimens. These cases are perhaps more frequent than we suppose, because one must think that these birds, too easily seen, are quickly eliminated by their enemies, all the more because they represent specimens of reduced vitality, since albinism implies degeneration."

Again this author says: "But the breeders are not content with modifying the coloration of the animals that we have just enumerated. The transformation has been more complete, and among others varieties have been created by alterations carried out upon the size, bodily form, or a part of the body, and the voice." Here Legendre recognized changes in morphology and behavior, but does not specifically associate them with pigment alterations.

Of particular interest is Legendre's description of the albino mutant of the Collared Dove, *Streptopelia roseogrisea*,—"We may note that aside from the Canary and the Undulated Parakeet, there have been domesticated few cage birds. It is always necessary to mention the Collared Turtledove, raised since long, but which scarcely interests the amateurs, because it always remains with its single white variety. This white variety was much studied in the past because of the gentleness of the bird. It was the symbol of faithfulness; and the gift of a white Turtledove to a lady much resembled a betrothal.—Occasionally there have been found in the same nest one youngster with gray plumage beside a white one."

CONCLUSION

A sample of ornithological literature and recent observations demonstrate that certain pigment variations in birds possess correlates in the modification of morphology, physiology, and behavior, as shown previously to be the case in mammals.

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Georgia State College for Women, Milledgeville, Georgia, July 11, 1950.

XXXIII

Faded Bronze Plumage: An Autosomal Mutant in the Turkey[1]

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(Received for publication November 18, 1948)

IN THE spring of 1947 a few and in 1948 a considerable number of "sports" appeared in the Broad Breasted Bronze flock of Mr. Robert K. Shearer, a Pennsylvania turkey breeder. Because these aberrant individuals were markedly smaller in body size than their contemporary normal-colored Bronze turkeys, this matter was referred to one of us (C.E.K.) whose interest in possible correlations between simply inherited mutant coat colors and morphology, physiology and behavior as factors in preadaption to domestication is well known.

In the fall of 1948 a trio each of mutants and "normal" colored Bronze were kindly furnished to the University of Georgia by Mr. Shearer. When circumstances made it impossible to obtain poults from these birds, Mr. Shearer, during the spring of 1949, made weekly shipments of day-old poults. Unfortunately, the already poor viability of the mutants is reduced by shipping so that it seems doubtful that sufficient adults can be reared to test the mode of inheritance of this mutation. Hence, it seems desirable to record the facts at hand pending further investigation of the problem.

The mutation appeared in the 1948 breeding season in the progeny of seven toms "predigree mated" to groups of hens ranging from 5 to 10 in number. It is significant that the hens within each group were half-sisters although of the 50 hens in these matings, only eleven produced mutant poults. There is no evidence that segregation for this trait reduced hatchability since hatchability of 749 eggs set from hens that produced "sports" was 86.7 percent of fertile eggs and fertility was 92.9 percent as compared to 88.0 percent and 73.2 percent, respectively, for the 2,297 eggs set from pen mates that produced only "normal" Bronze poults.

Approximately 150 faded birds hatched, of which 70 survived to September 1st.

[1] Expenses incurred in this study have been covered in part by a grant-in-aid to the senior author by the Rockefeller Foundation for Medical Research.

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Mortality on the home farm approximates 50 percent for the mutants as compared to an average mortality of 10 percent for "normal" colored Bronze. Of poults shipped to the University of Georgia, 80 percent failed to survive to 10 days of age as compared to 12 percent of the "normals."

The mutant poults are small and weak. The down pattern is of the typical bronze type but is faded to a reddish-brown color. The down is noticeably shorter than normal especially on the head. The pigment of the iris is less dense than normal with a definite pinkish cast and the beak, shanks, toes and claws are pinkish white rather than heavily pigmented. In older birds the feathers show the typical bronze markings but in a dilute brown with an overall reddish tinge.

The newly hatched poults behave in the manner described by Hutt (1935) as characteristic of blindness in chicks. There are slow movements of the head from side to side and pecking is poorly directed and coordinated. Further evidence of blindness is seen in the frequent circling movements but, in contrast to Hutt's stock, a pupillary reflex follows exposure to strong light.

At all ages the plumage is rough in appearance due to many broken or missing feathers. The faded adults are weak and sluggish in appearance. The tom was

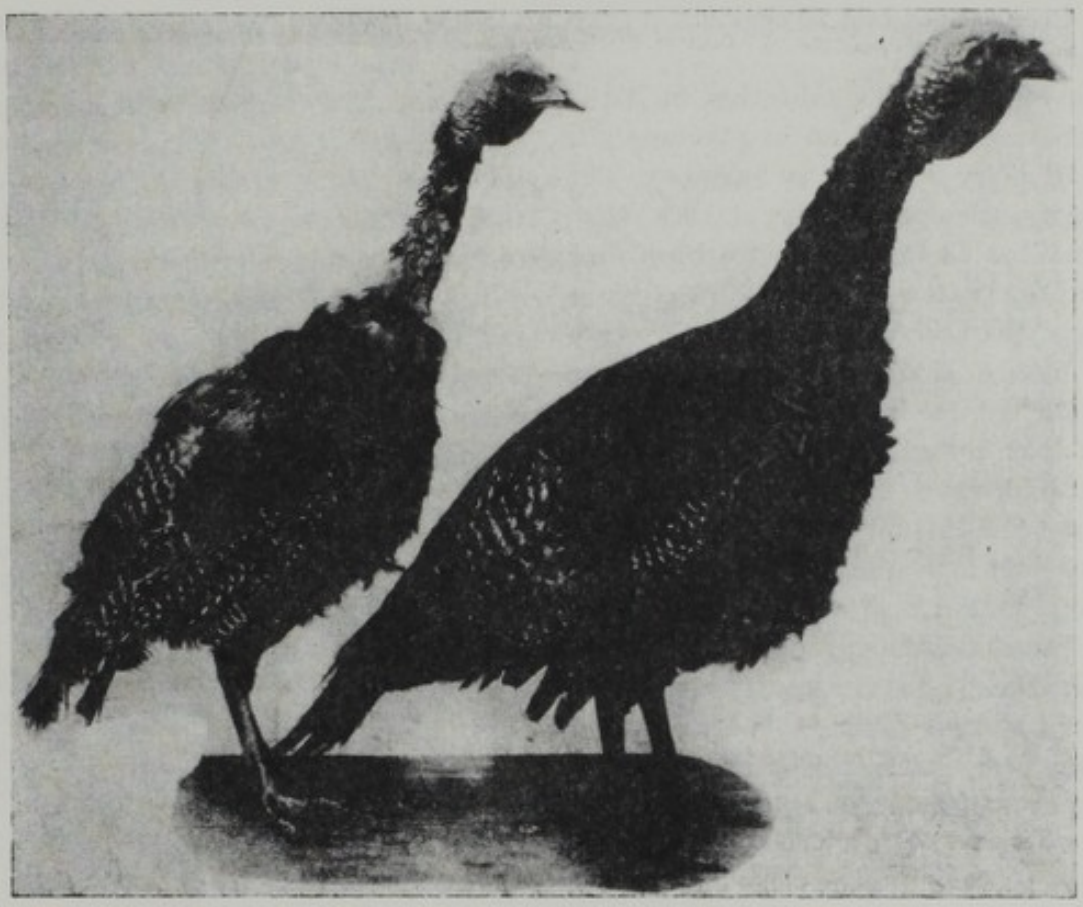


FIG. 1. Faded and normal Bronze hens. Faded Bronze have typical Bronze plumage pattern except that the black and brown pigment is much diluted and has a reddish tinge. The plumage is characteristically "rough" in appearance. Pigment of the eye is less dense than normal with a definite pinkish cast although there is some variation among individual specimens. Note the relative lack of pigment in the shank and toes.

never observed to gobble or tread and this observation has been confirmed by Mr. Shearer as characteristic of the birds on the home farm. The two hens did not lay any eggs up to December 24th when theft of all the birds abruptly terminated our observations although the two "normal" Bronze hens laid 20 eggs during this period.

The effect of this mutation on body weight is so marked as to preclude the need of body weights as evidence. The mutants are significantly smaller than "normal" at all ages and, in the birds now under observation at the University of Georgia, the heaviest mutant is, in every case, lighter than the slowest growing "normal" of the same age. It has been noted that the differential in weight between mutants and "normals" decreases with age but this may merely result from the survival to maturity of only the most vigorous mutants. A correlation between body size and a color gene has been previously described in chickens. Maw (1935) reported linkage between the sex-linked gene for silver and factor(s) for large body size and significantly longer bones although the differences are not of the magnitude found in the present study.

Evidence of the mode of inheritance of faded Bronze mutant must await actual breeding tests. Of the known mutants of the turkey the present case resembles most the sex-linked, recessive, imperfect albino described by Hutt and Mueller (1942) except that plumage color is less restricted and there is more pigment in the eye. Asmundson (1945) has reported a sex-linked recessive brown in the Bronze turkey. However, distribution of the sexes of the mutant poults in the present case is in reasonable agreement with a 50–50 sex ratio which obviates a sex-linkage hypothesis. The available evidence suggests that faded Bronze is due to an autosomal recessive factor(s).

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These "faded" turkeys break humerus, radius, ulna, wrist and finger joints more frequently than do the normals. They apparently have calcium deficiency in the bones because they have "green stick" fractures. The weak feather structure is most noticeable on the last two primary feathers. The body contour feathers of faded turkeys show little bronzing or iridescence. The wing feathers appear dry, the rachis splits, and barbs often break off at the rachis.

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XXXIV

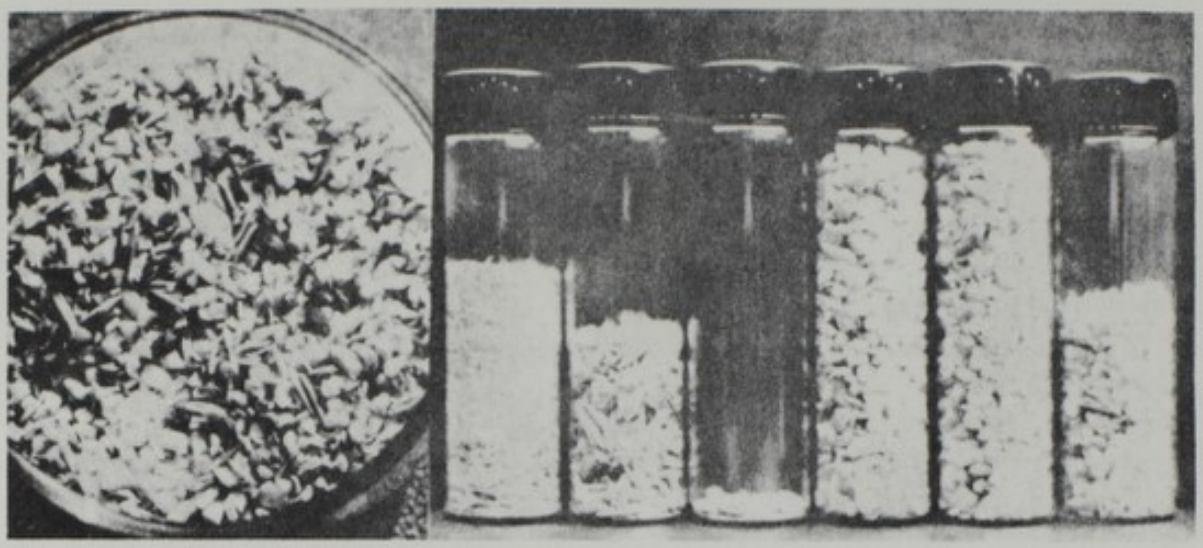
ALBINISM AND DIET CHOICE IN THE RING NECK DOVE

Clyde F. Keeler*

A NUMBER of years ago I observed that if a balanced diet in pellet form was fed by means of a dispenser to several coat color mutant strains of Norway rats derived from a single wild gray strain, the various strains consistently chose a different quantity of food. This is in accord with the finding of H. H. Donaldson that rats of mutant strains differ from the wild gray strain[1] in size of various glands, including thyroid, and therefore we might expect them to have different metabolic requirements.

Later the matter was tested further by allowing rats of derivative mutant coat color strains to eat wheat bread (white, unenriched), lard, and a series of vitamin pills, each vitamin being offered in a separate pill. The two mutant strains that were studied balanced their diets differently in comparison with the wild gray strain from which

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ALBINO REJECTION

Figure 14

Food rejected by albino doves. Left—The undisturbed food dish; Right—The sorted reject. The bottles contain respectively: screenings, oat hulls, wheat, cracked corn, cracked corn and cracked corn.

they were derived. As laboratory facilities were not available, extensive and detailed studies were abandoned.

Because these observations were meager, this work has never been published, but it was hoped that someday a series of related experiments could be carried out on the subject and the data studied statistically.

For seven years I have maintained a few pigmented specimens of the Northeast African dove, *Streptopelia roseogrisea*, as well as a few albino mutants of this species. The two forms differ markedly in their ability to fly. The grays take off like wild birds whereas the albinos flutter, having little energy.

During the time that I have observed these birds, the albinos tended to choose a diet differing from that chosen by the gray doves when both were fed scratch feed consisting of corn, wheat, kafir and oats. I could observe this difference only because I kept albino and gray pairs caged separately. It should be pointed out that if one keeps albino and gray birds together, as is usually done, the scratch feed will all be eaten up and the difference in choice of diet will probably not be noticed.

Since I constantly kept more food in their dishes than they would eat, thus allowing them to choose their diets, the food dishes always contained some rejected materials after a period of feeding. Because the rejected materials had a different appearance, it was decided to compare the diet chosen by a pair of albinos with that chosen by a pair of grays. It is evident from the photographs (see Figures 14 and 15) that the albinos ate wheat, hulled and ate oats, but rejected cracked corn. The gray pair ate the corn, but rejected the wheat and oats. The exact amounts found in the rejects are shown in Table 1.

Because the rejects were from a feed mixture theoretically containing equal amounts of wheat and corn, we have used 62.84 grams (average of 59.67 and 66.01) as the theoretical expectancy for both wheat and corn that should be found in equal proportions in the rejects if no selective mechanism were operating.

The albinos rejected 59.67 grams of corn and 0.77 grams of wheat. The chi-square for this deviation from equality is 62.23 indicating a very high probability that selection took place, a chi-square as large as 6.63 indicating a probability of only .01 that the deviation was due to chance alone.

The normal gray doves rejected 2.32 grams of corn and 66.01 grams of wheat. The chi-square for this deviation from equality is 58.45 indicating a very high probability that selection took place.

The greater amount of screenings in the albino

TABLE I. Rejected food of albinos and normals by type and weight

	Screenings	Oats	Wheat	Cracked corn
Albino reject	8.45*	3.54 (hulls only)	0.77	59.67
Normal reject	3.83	6.14 (whole grains)	66.01	2.32

* All amounts given in grams.



GRAY REJECTION

Figure 15

Food rejected by gray doves. Left—The undisturbed food dish; Right—The sorted reject. The bottles contain respectively: screenings, whole oats, wheat, wheat, wheat and cracked corn.

reject probably indicates their greater activity in eating the scratch feed, and is in keeping with the fact that the albinos tended to hull and eat the oats whereas the grays tended to reject the whole oats.

A number of possible explanations may be offered. Physical differences in ability of the gizzard to grind the grain, metabolic differences demanding a unique diet, reduction of pigment in the albino eye so that colors appear different (assuming that color vision controls choice), roughness and size differences (if these factors control choice), may all be envisaged. No immediate cause of this correlation can be stated with certainty.

Summary

Albino doves were found to eat wheat and oats but reject cracked corn. Gray doves ate cracked corn but rejected wheat and oats. Both types ate kafir. The reason for this differential choice of diet has not been determined.

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XXXV

THE SEARCH FOR MOON-CHILD ALBINOS

It was raining at the small Paitilla Airport as it had been doing for twenty-four hours in the drenched and temporarily dismal city of Panama. It is sometimes like that during the wet season. I stood in the hanger with my baggage. I walked around nervously, pulled up my coat collar, and waited impatiently. I looked at my watch. It showed seven-thirty. The officials said no planes would venture out that day, but I had no other place to go. So I waited on and on.

About 10:30 A.M. there was a rift in the clouds. The sunlight poured through, and the pilot said he would try it with the little red-and-yellow Piper Cub; so we quickly rolled out the tiny plane, raced our small engine and zoomed up through a few white-fringed, cumulus formations. We sped down the Pacific Coast with its dark pencil line waves chasing each other over the surface of the gray sea, to disappear one after another upon the hazy shore. A plane from a rival company roared off the field and followed us through the bank of small, cottony wisps into which the enormous black rain clouds were rapidly separating.

We climed 75-100-150-200-250 feet as we flew down the coast. Twenty-five miles from Panama City we pointed the Cub almost due east where the clouds were dense, black, and foreboding. "The other plane turned back," said the pilot.

The clouds suddenly lost their cumulus formation. They dissolved and we were swallowed up completely in a torrent of blinding rain. The water washed over our windshield as though we were plowing along the depths of a mighty river. Sudden flashes of lightning split into a thousand pieces the neutral gray, water medium through which we were boring, and the Cub rocked and shivered with the crashes of thunder.

"I'm lost, called the pilot, trying to make his voice carry above the noise of our engine. "I guess we should have turned back."

"Well why don't you turn back if the weather is too bad?" I yelled in reply.

"It's too late now. We're over the jungled Cordillera and there are no instruments on this plane".

On and on through lightning and water the monotonous engine roared. We climbed up and up into the grey uncertainty before us. The moments were tense.

"I hope we are not off our track because there are two peaks and we must fly between them," said the pilot

I knew what would happen if we were off the track; so I did not ask. I just hoped and prayed that we were on the track. Further and further we groped blindly through the water and each moment seemed like an hour. We were expecting at any instant to feel the sudden crash of our Cub in some tall jungle tree. I had never felt so close to eternity.

The pilot had been straining his eyes to differentiate the neutral gray avalanche of water before us. He kept peering this way and that, and at last he said: "I think I see a V over there. I hope I'm right, because if I am it is the mountain pass between the two peaks." I fervently hoped that he was right, as we made for the half-imagined V. As luck would have it, he was correct, and a few minutes later we swept between the gray, cloud-covered peaks A little more time and we burst out of the water into the golden sunshine of a crystal clear day on the beautiful San Blas coast.

We followed the shoreline with its coconut plantations, skimming gayly over the trim little brown cane-and-thatch Indian towns of Narkana, Tikantiki, Tupili, and the rest. Dozens of green, palm-fringed atolls glowed in the sunshine like so many miniature Paradises.

At Ailigandi we put down on the mainland, dropped myself and my baggage among a dozen colorfully dressed, exotic-looking native women and girls, and the aviator was off again. Among them was a moon-child girl. That was encouraging since I had come to Panama to study the moon-children.

"Iki pe nuka?" asked a woman through her big, golden nosering. I had expected to find someone who could speak Spanish, English, French, German or Latin. But no, for the first time in all my travels words failed me

"Pia pe neka?"

That didn't register either, nor did the final question: "Ipua?"

Realizing that we were getting nowhere, the woman and her daughter deposited my bags in their dugout and I made an embarrassing demonstration of my ignorance of how to get into a canoe. They paddled me to the Island of Ailigandi, and as we approached I saw an old Indian woman jumping up and down on the shore, brandishing her bony fists and screaming angrily at me.

"Maldita" said the woman in front of me in Spanish as she turned her head and smiled behind her nosering, while nodding indicatively toward the enraged woman at the water's edge.

When we had passed my welcoming committee of one, and her screams had died down, the woman and her daughter brought the canoe to shore and I stepped out to shake hands with a smiling, brown-skinned Indian in neat American clothes. It was Alicibiades Iglesias, the native Cuna Indian Missionary who was

educated in New York and Iowa, and whose Christian school is well known to thousands of people in the Canal Zone and in the United States.

About Alcibiades and myself there soon collected a swarm of lively, inquisitive Indian boys, some naked and some in short trunks. They were soon joined by a few girls in colorful molas and golden nose rings.

Among these youngsters were two of the many Cuna Moon-Child albinos that I had come to study.

XXXVI

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THE GEORGIA ACADEMY OF SCIENCE

The Caribe-Cuna Moon-Child: A Demonstration of Pigment-Gene Pleiotropy in Man

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(Accepted for publication September 12, 1950)

In 1941 one of us (C.E.K.) showed that certain genes, known to modify melanic pigmentation in the Norway rat, also bring alterations of morphology, physiology and psychosomatic behavior.[1,2] Since that time this phenomenon has been demonstrated in other mammals,[3] birds[4] and fish.[5]

Although pigment-gene pleiotropy will probably be identified someday in other human variations such as Albinos and Red Heads, it is realized that samples of these variations taken from such a group as the American population, present the great disadvantage of heterogeneous residual hereditary background, due to hybridity and diverse origin of different individuals composing the sample. Such heterogeneous residual hereditary backgrounds may be expected to obscure many developmental tendencies of the pigment genes in question, that would stand out distinctly on an inbred, residual hereditary background. Again, we cannot be certain that all variants in a Red Head sample, for instance, represent but one genetic entity.

The albinistic Caribe-Cuna Moon-Children, familiar to one of us (L.P.) as patients over a period of years, have the advantage of a high gene frequency within an inbred population, and therefore they would be expected to show pleiotropy distinctly if it is present. In addition, the Moon-Children undoubtedly represent a single genetic entity. These facts make the Moon-Children a genetically superior material in which to search for pigment-gene pleiotropy in man.

For the benefit of any persons who might misinterpret the findings of our present study, we desire to state that in no way whatsoever, is this an investigation of race problems or a comparison between races, but merely the study of a simply inherited, albinistic syndrome segregating in an inbred population.

During the summer of 1950 we have examined thirty-seven Moon-Children.

Measurements of height and weight show that the Moon-Children are slightly shorter and lighter than are normal Cuna Indians. Head shape of Moon-Children appears to be brachycephalic in a higher percentage than normal, but this has not been proven.

The skin in general lacks all pigment, is horribly blistered by short exposures to sunshine to which it also responds by producing scat-

tered blotches of pigment as in true albinos. The skin may develop benign tumorous growths in a few cases. The skin becomes much wrinkled by ten years of age, especially on the back of the neck, and this condition increases with age. The skin, from the age of about one and one-half years, is covered with severe sores, due to infection of wounds, abrasions, and insect bites. The skin is very dry. The lips are enlarged and protrude.

Head hair at birth is usually white, changing through tow, to a rich golden in youth, and then to light brown, or even reddish brown in middle life. We have hair samples for study, and although all the comparisons have not yet been made, it would appear that the diameter of the hair of the Moon-Child is smaller than that of normals. It blows about more freely in the breeze.

Although normal Cuna are very smooth skinned, the Moon-Children bear straight, white hair on their bodies which on the forearms and lower limbs may measure from one-fourth inch to one inch in length by the age of nine years. This amazing hair was found on the appendages of all thirty-seven specimens examined.

The eyes tend to be of the oriental type in which the eyelids are invisible when the eye is open, whereas this kind of eye is fairly rare among normal Cuna. Part of this tendency may be due to maintaining skin muscles about the eye tense in an attempt to shut out more light. The area about the eyes often appears swollen or enlarged. Eye color is a rich blue, a much deeper blue than seen in true albinos, with some black around the periphery and a yellow or buff band developing about the pupil at the age of six or seven years. Moon-Child eyes examined ranged from five months to sixty years of age. Moon-Child eyes are weak and lateral nystagmus is present at all intensities of light under which they were examined—even down to the dim twilight of the Cuna hut.

We have been unable to determine basal metabolisms, but the indications are that metabolic rates of Moon-Children are reduced. Some specific gravities have been taken on urine samples and these are very low. Ultra-violet spectrum analysis of urine samples shows some substance, probably a product of purine metabolism, to be reduced in quantity, or possibly missing entirely. Moon-Children do not appear to have an incidence of lung infection above normal, but they constantly carry colds of the nose, head, and throat. Readings were taken with a manual dynamometer which show the Moon-Children are reduced in strength in both males and females. They have a slow gait, and slow movements. The physical directors of four schools say that Moon-Children lack endurance in physical

contests. Because this lack of endurance is common knowledge, the town does not call upon them for heavy physical labor in community projects, and the home demands from them only the lightest of duties.

Moon-Children, according to the observation of one of us (L.P.), are slow in developing sexually. Among the females, menstruation begins later than normal and the breasts are smaller in general. Males are undersexed, and although tradition forbids them to marry, they never have been known to make advances or sex attacks as normal males would under the restrictions of a rigid town government that makes prostitution impossible, except in one or two of the fifty Cuna towns.

The voices of Moon-Children tend to be soft, and this is particularly noticeable in adult males.

The mentality of Moon-Children appears to be normal, and no less than fourteen of them have competed in formal school classes. The chiefs of two large Cuna towns, Ailigandi and Ustupo, as well as other residents, tell us that Moon-Children tend to be stubborn and hot-tempered. Most Moon-Children seldom smile, and when they do, their smile is usually feeble. They definitely lack expression in the face.

It is noteworthy that Moon-Children do not want to associate with each other, and at the age of twelve or thirteen (when the Moon-Child girls find their normally pigmented friends marrying and having babies, and Moon-Child boys realize that they cannot compete physically with other boys) they often cease to associate with normals and become non-social. This tendency appears to be due to their feeling of inferiority.

However, in spite of this tendency to solitude, Moon-Children may have a strong, personal determination to succeed. For example, one Moon-Child girl of twenty years who had not had a day of schooling previously, persisted through three weeks of night classes until she had learned pronetic reading better than those normals who had four weeks training. One Moon-Child of eleven years, finding that he could only squeeze eight kilos on the manual dynamometer, whereas his associates could squeeze twelve kilos, returned alone half-a-dozen times each day during four weeks, determined to better his record. Such persistence has allowed Moon-Children to become leaders in their community in spite of their physical handicap.

Previously, the inheritance of the Moon-Child variation was obscure, its occurrence being considered as the segregation of a Nordic blond gene in one instance and in another it was considered as sex-linked. Many Cuna believe the variation due to diet or to maternal impressions caused by the mother-to-be having gazed too frequently at the moon. From the data now available, there is no doubt but

that the Moon-Child gene is a simple recessive, unit-character, giving normal mendelian ratios. In simplex it produces lighter colored individuals than normal in many cases, and it appears to be either a higher allel of the albino gene or else a mutation at an independent locus.

Details of this work will be published in the future.

The authors wish to thank Dr. H. Heinmets for making the ultraviolet spectrum determinations on urine samples mentioned in this paper.

They are indebted to the Rockefeller Foundation for a grant-in-aid to the senior author which has made this study possible.

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XXXVII

AN ATTEMPT TO ELIMINATE A GENETIC SYNDROME IN MAN

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EDITOR'S NOTE: *In 1941 Dr. Clyde Keeler (in the* Journal of Comparative Psychology, *34:241-250) showed that certain genes that modify melanic pigmentation in the Norway rat also affect morphology, physiology and psychosomatic behavior. Since that time this phenomenon (a form of pleiotropy) has been demonstrated in other mammals, birds and fish. Recently, September 1950, Dr. Keeler and Dr. Luis Prieto, a physician practicing in Panama, have published in the* Bulletin of the Georgia Academy of Sciences *(VIII, No. 3) a paper, "The Caribe-Cuna Moon-Child: a Demonstration of Pigment-Gene Pleiotropy in Man." In that paper the authors predict thta someday pigment-gene pleiotropy will be demonstrated in other human variations, such as Albinos and Red Heads. But samples of these taken from the American population present the great disadvantage of heterogeneous hereditary background, due to hybridity and diverse origin of the different individuals. The Cuna Moon-Children have the advantage of high gene frequency within an inbred population, and therefore would be expected to show pleiotropy distinctly in a number of specific characteristics.*

Many scientists take it for granted that simply inherited pigment variations of mammals and man are in no way related to variations of morphology, physiology, and psychosomatic behavior. A few will visualize simply inherited morphological variations being rarely associated with certain pigment alterations, providing that their determining genes are linked. that is, reside at different loci in the same chromosome.

Psychologists and sociologists in particular seldom admit the possibility of pleiotropic effects stemming from the presence or activity of a single gene substitution in such a fashion as to eventually alter characteristics of morphology, physiology and psychosomatic behavior in the same individual.

And yet, Darwin and others of the old school recognized such associations of characteristics on the morphological level (including coat pigmentation) with traits of physiology, and H. H. Donaldson in his later years (unpublished) recognized that various coat color mutations were associated with less vigorous growth and a tendency to incomplete development of various organs in the Norway rat.

In spite of all the present opinion to the contrary, Dr. Keeler has published data on pigment variations and their correlates in fish, birds and mammals during the past ten years. On the basis of these data he maintains that pigment gene pleiotropy does *exist in these forms and that in them it* does *affect morphology, physiology, and psychosomatic behavior.*

If this is true, then pigment gene pleiotropy may possibly turn out to have important implications, as Dr. Keeler believes. (1) It ought to be possible by selecting and combining the requisite coat color genes, to produce tamer strains of certain animals that now, because of wildness and nervousness, destroy millions of dollars worth of young for the fur ranchers annually. (2) Theoretically, at least, pigment gene pleiotropy seems to offer a part-solution to the problem of domestication in general. Darwin noted that coat color variations were common in most domesticated stocks, but he never suggested that coat color variations might share as causes of domestication. On the contrary, Darwin felt that the coat color variations themselves were the result of domestication. (3) Pigment gene pleiotropy should permit the selection of pigment-associated syndromes of temperament and psychosomatic behavior for study in the laboratories of experimental psychology. The next few years should give opportunity to test these predictions.

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If such correlates are present in man they may have psychological and medical import. Blonds are reported to be deficient in their use of vitamin A. Redheads are believed to be hypersensitive to anaesthetics and narcotics. Because of this latter belief certain hospitals now use different anaesthetics and lighter dosages for Redheads. Redheads, in general, are said to suffer more quickly from heat exhaustion than average individuals. If this is true, it might have military application. Ordinarily, we have laughed off the alleged temper and sensitivity tendencies of Redheads.

In this issue of EUGENICAL NEWS *Dr. Keeler describes the Moon-Child variation found among the Caribe-Cuna Indians of Lower Panama. This variation definitely exhibits pigment gene pleiotropy. And because the Moon-Child variation demonstrates that pigment gene pleiotropy is true for man upon the levels of morphology, physiology, and psychosomatic behavior, we will be forced to re-examine other simple pigment variations of man in a serious and detailed fashion.*

The colorful Caribe-Cuna Indians with their golden nose-rings and interesting devil appeasement ceremonies, have warded off civilization rather successfully for 450 years and they have also battled with a problem of eugenics for many centuries. In the latter battle they are losing ground.

The eugenic problem of the Caribe-Cuna is presented by the fact that they have a high incidence of albinistic Moon-Children. This Moon-Child variation is described in detail by Keeler and Prieto from whom we shall take the most of the following description.

Measurements of height and weight show that the Moon-Children are slightly shorter and lighter than are normal Cuna Indians. Head shape of Moon-Children appears to be brachycephalic in a higher percentage than normal, but this has not been proven. The facial angle tends to be depressed. Hands are often small and soft.

The skin in general lacks all pigment, is horribly blistered by short exposures to sunshine to which it also responds by producing scattered blotches of pigment as in true albinos. The skin may develop benign tumorous growths in a few cases. The skin becomes much wrinkled by ten years of age, especially on the back of the neck, and this condition increases with age. From the age of about one and a half years, it is covered with severe sores, due to infection of wounds, abrasions, and insect bites. The skin is very dry. The lips are enlarged and protrude.

Head hair at birth is usually white, changing through tow, to a rich golden in youth, and then to a light brown, or even reddish brown in middle life. We have hair samples for study, and although all comparisons have not yet been made, it would appear that the diameter of the hair of the Moon-Child is smaller than that of normals. It blows about more freely in the breeze.

Although normal Cuna are very smooth skinned, the Moon-Children bear straight, white hair on their bodies which on the forearms and lower limbs may measure from one fourth inch to one inch in length by the age of nine years. This amazing hair was found on the appendages of all thirty-seven specimens examined.

The eyes tend to be of the oriental type in which the eyelids are invisible when the eye is open, whereas this kind of eye is fairly rare among normal Cuna. Part of this tendency may be due to maintaining muscles tense about the eye in an attempt to shut out more light. The area about the eyes often appears swollen or enlarged. In general, eye color is a rich blue, a much deeper blue than seen in true albinos, with some black about the periphery and a yellow or buff band developing around the pupil at the age of six or seven years. One baby girl with reddish hair showed a violet tinge to the eye color, and several have brown eyes. Moon-Child eyes are weak and lateral nystagmus is present at all intensities of light under which they were

examined—even down to the dim twilight of the Cuna hut (.8 to 1.6 foot candles).

We have been unable to determine basal metabolisms, but the indications are that metabolic rates of Moon-Children are reduced. Hands are often cold and clammy. Some specific gravities have been taken on urine samples and these are very low. Ultraviolet spectrum analysis of urine samples from boys show some substance, possibly a steroid esterone, to be reduced in quantity, or missing entirely. The Moon-Children do not appear to have an incidence of lung infection above normal, but they constantly carry colds of the nose, head and throat. Readings were taken with a manual dynomometer which show that Moon-Children are reduced in strength in both males and females. They have a slow gait, and slow movements. The physical directors of four schools say that Moon-Children lack endurance in physical contests. Because this lack of endurance is common knowledge, the town does not call upon them for heavy physical labor in community projects, and the home demands of them only the lightest of duties.

Moon-Children are slow in developing sexually. The voices of Moon-Children tend to be soft, and this is particularly noticeable in adult males.

The mentality of Moon-Children appears to be normal, and no less than fourteen of them have competed in formal school classes. The chiefs of two large Cuna towns, Ailigandi and Ustupo, as well as other residents, tell us that Moon-Children tend to be stubborn and hot-tempered. Most Moon-Children seldom smile and when they do, it is usually a feeble smile. They definitely lack expression in the face.

Thus, the Moon-Child represents not merely a pigment variation, but rather a pleiotropic syndrome affecting morphology, physiology and psychosomatic behavior.

Moon-Children "sin less" than other Cuna do (possibly a correlate of low metabolism), and are in special favor



Albinistic Moon-child from Ailigandi, a village of the Caribe-Cuna Indians of Lower Panama. Note photophobia, pigment blotches, and protrusion of the lips.

with the Great Spirit (Pap Tummat), to whom they shout prayers for the town upon occasion. They must shoot the sky-dragon that is swallowing the sun or moon at times of eclipse, and have special houses in heaven. In spite of this unique position in the Caribe-Cuna culture, they have been looked upon as somewhat monstrous and unfortunate, and their elimination from the tribe has been considered for centuries as the natural object of eugenic measures.

There are various stories that account for the origin of Moon-Children. Some Indians invoke maternal impressions to explain their occurrence, because the Cuna believe that all sorts of markings may be due to the mother-to-be or her

husband having looked at the wrong things. When Moon-Children are produced one or both parents may have gazed too long at the moon, cotton or other white objects. Chief Ikwanidipippi of Ailigandi believes that the production of Moon-Children is due to diet.

Columbus and his sailors may have been the first white men to have seen Caribe-Cuna Moon-Children. The English pirate, Wafer, who described them in great detail says that the Indians of his time credited Moon-Children to be the descendants of the first chief of the Caribe-Cuna tribe, himself a Moon-Child. This story may refer to Nele Sipu (The Moon-Child sage), one of the 8 cultural heroes of the race who floated down from heaven each on a huge disc. It was this same Nele Sipu who said that "all men are brothers." Although we do not know exactly when the Moon-Child mutation occurred, it must have been early in the history of the Caribe-Cuna or it could not have spread so widely by Wafer's time, and would not have been almost universally distributed today.

Keeler and Iglesias have collected pedigrees that confirm what was previously suspected, namely, that the Moon-Child variation is due to a mutant gene in duplex, and that this same gene in simplex frequently produces a pigmentation lighter than that of the average Indian.

To the Cuna, constantly struggling to obtain his deficient food supply, infanticide as a method of eliminating the physically handicapped of the tribe does not strike the conscience with such horror as it does that of the more fortunate American of European descent.

Alcibiades Iglesias, the famous Cuna missionary, says that when he was a boy on the Island of Nargana, his mother would occasionally come home and say, "The midwives buried Sipu (The Moon-Child infant)." And in his childhood innocence and curiosity he would ask, "But, mother, why did the midwives bury Sipu?" To this she would reply, "Because the midwives felt sorry for Sipu."

Thus, from earliest times the Cuna appear to have eliminated most of the albinistic Moon-Child homozygotes by means of infanticide possibly on the grounds of sympathy for them, knowing well the handicap under which they would have to live. Because of the feeling that they were somewhat monstrous, and for fear that they would beget others like themselves, the marriage of the surviving Moon-Children was taboo for centuries. That some did have children during Spanish colonial times, however, is recorded by Salcedo, and in pirate days, is recounted by Wafer.

Today very few Moon-Child men marry, and practically none of the Moon-Child women. Should these latter marry, it is said to be without ceremony, although Moon-Child girls do receive the customary puberty rites of the tribe.

Thus, infanticide and town restrictions on marriages have tended to hold down the spread of the Moon-Child gene within the germplasm of the tribe, but other factors have tended to counteract these eugenic measures.

The Caribe-Cuna population has been variously estimated at between 400,000 and 700,000 when Columbus' men invented the "game" described by Peter Martyr d'Anghera. This consisted of catching Caribe-Cuna Indians and of whacking off their heads to see who could decapitate them with the fewest blows. The Indians retaliated by eating some of the Spaniards. Then followed the bloody campaign of the conquistadores for the extermination of the Caribe-Cuna tribe. A great slaughter of the Cuna took place, and a remnant fled to the jungle covered mountains on the north side of the San Blas Cordilleras that were already inhabited by Caribe-Cuna. All were killed south of the mountains. After pirate days the Cuna spread. Some of them ventured to build towns down on the Caribbean shore, and subsequently on the coastal atolls. Today the tribe numbers something over 20,000.

Their fear of everybody, including people from other towns of their own tribe, has tended to make each town a closely knit, inbreeding unit. There are

today a few inter-island marriages, and occasional island-mainland alliances, but most marriages are between persons born, raised and living all their lives in the same town. Curiously enough, Moon-Children are present or have been born in nearly every island town.

The great reduction in numbers of the total population of the tribe together with the town-inbreeding pattern has spread the Moon-Child gene to a greater percentage of inter-marrying families making random matings more frequent between heterozygotes. And these more frequent heterozygous marriages have increased the incidence of Moon-Child births.

Two factors, due to civilization, are helping to weaken the eugenic measures taken by the Cuna Indians to keep down the incidence of Moon-Children. The Indians have learned that civilized peoples are very much against infanticide, and consequently, on such enlightened islands as Ailigandi and Nargana infanticide is rapidly disappearing. We have listed 13 living Moon-Children whose home is Ailigandi and 14 others born at Nargana. With the impact of democratic civilization has come an increased emphasis upon the rights of the individual as opposed to the authority of the town council, and hence a young Moon-Child man in Nargana or Ailigandi may now argue his individual right to marry, whereas formerly he took the decision of the town council and of tradition in silence. Again, under strict control of the town council, the Moon-Child girl never dared to have illicit relations, but we have recorded six Moon-Child girls who have illegitimate children today.

The indications are that unless the present tendencies are reversed, the Moon-Child incidence will continue to increase among the Caribe-Cuna Indians. However, if the handicap were considered great enough, the incidence could be much reduced by voluntary abstinence from childbearing, because many heterozygotes have a lighter skin color than the average Indian, as we have noted above. Whether the tribe will ever undertake such a general restriction of marriage on eugenical grounds is problematic.

The author is indebted to the Rockefeller Foundation for a grant-in-aid that has made this study possible.

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XXXVIII

THE CARIBE CUNA MOON-CHILD AND ITS HEREDITY

CLYDE E. KEELER*

DURING the summers of 1950-51-52 I studied the albinistic Moon-children among the primitive Caribe-Cuna Indians of San Blas Province, Lower Panama, with special reference to morphology, physiology, behavior and heredity. These Cuna Indians are noted not only for their big, golden nose rings, colorful appliqued cotton blouses, strange customs and universal devil appeasement ceremonies, but also for the fact that they possess the highest incidence of albinism in the world.

My studies were undertaken in order to determine whether or not the types of correlation that I had found to exist in fish, birds and mammals between certain coat color mutations and trends of morphology, physiology and behavior, exist also in man.

The Cuna Indians are an inbred people and hence possess a relatively uniform residual heredity background suitable for demonstrating well the pleiotropic effects of a single gene substitution. They have a great fear of outsiders, and a hatred for hybrids. When occasional alliances had been made in the 16th, 17th and 18th centuries, they massacred the foreigners and their hybrid children. The same thing happened again in 1925 when recent unions had taken place with Panamanians sent to police the towns that lie upon their palm-fringed atolls which skirt the Caribbean coast from east of Colon to well beyond the Colombian border. Ordinarily, no foreigner is permitted on these islands after sundown.

By associating myself with a project to reduce the Cuna spoken language to phonetic writing, and having undertaken the publication of a phonetic primer, I gained status, and most of the Indians lost fear of me. Consequently, in 1951 and again in 1952, I was permitted to visit nearly every inhabited Cuna island in company with the native Protestant Missionaries of Ailigandi, Mulatupu and Ustupo.†

Aside from the propositi, several hundred other Moon-children appear in the pedigrees collected.

Morphology

At birth, the Moon-child skin in general lacks all pigment. The complexion of Moon-children is whitish, pink, or florid. Its skin is horribly blistered by short exposures to sunshine to which it responds upon healing by producing scattered blotches that may be occasionally as large as three centimeters in

*Georgia State College for Women, Milledgeville. This paper is a brief account abstracted from a sixty-page manuscript of the same title awarded the research prize of the Association of Southeastern Biologists in 1952. The study was made possible by a grant-in-aid from the Rockefeller Foundation.

†Alcibiades Iglesias, Peter Miller, Frank Wilbur, Atilio Rivera, Claudio Iglesias, Jaime Rodriguez, and José Perez have escorted me, served as interpreters, and helped me in ways too numerous to mention. John Mason, American Missionary, and James Davis, native, made it possible for me to visit the islands of the Mandinga Bay Area west of Nargana.

In all, 152 Moon-children were identified. Most of them were examined in the large towns of Nargana, Tupili, Ailigandi, Ustupo, and Mulatupu. Sex, age, island of birth, island of migration and pedigrees of each Moon-child were procured as completely as possible.

The towns in which Moon-children were recorded are as follows: Narraskantup tummati, Soledad (Mandinga), Ikwanna, Orrostup, Akwatup, Arritup, Tupeor, Nusatup, Naluneka, Upikantup, Rio Cedra (Urkanti), Mormakketup, Riasuka, Nargana (Yantup), Corazon de Jesus (Nusatup), Tigre (Achumikur), Tikantiki (Nusatup), Playon Chico (Rio Okupseni, Moron, Kanirtup), Makepkanti, Tupili, Ailigandi, Mammitupu, Achutupu, Ustupo, Napikanti, Sassarti, Mulatupu, Tuwala, Karet, Achukunu, Arkia, Pukro, Tapalisa, Sokopti, Morti, Wala, Pirea, Ikanti. (See Figure 4.)

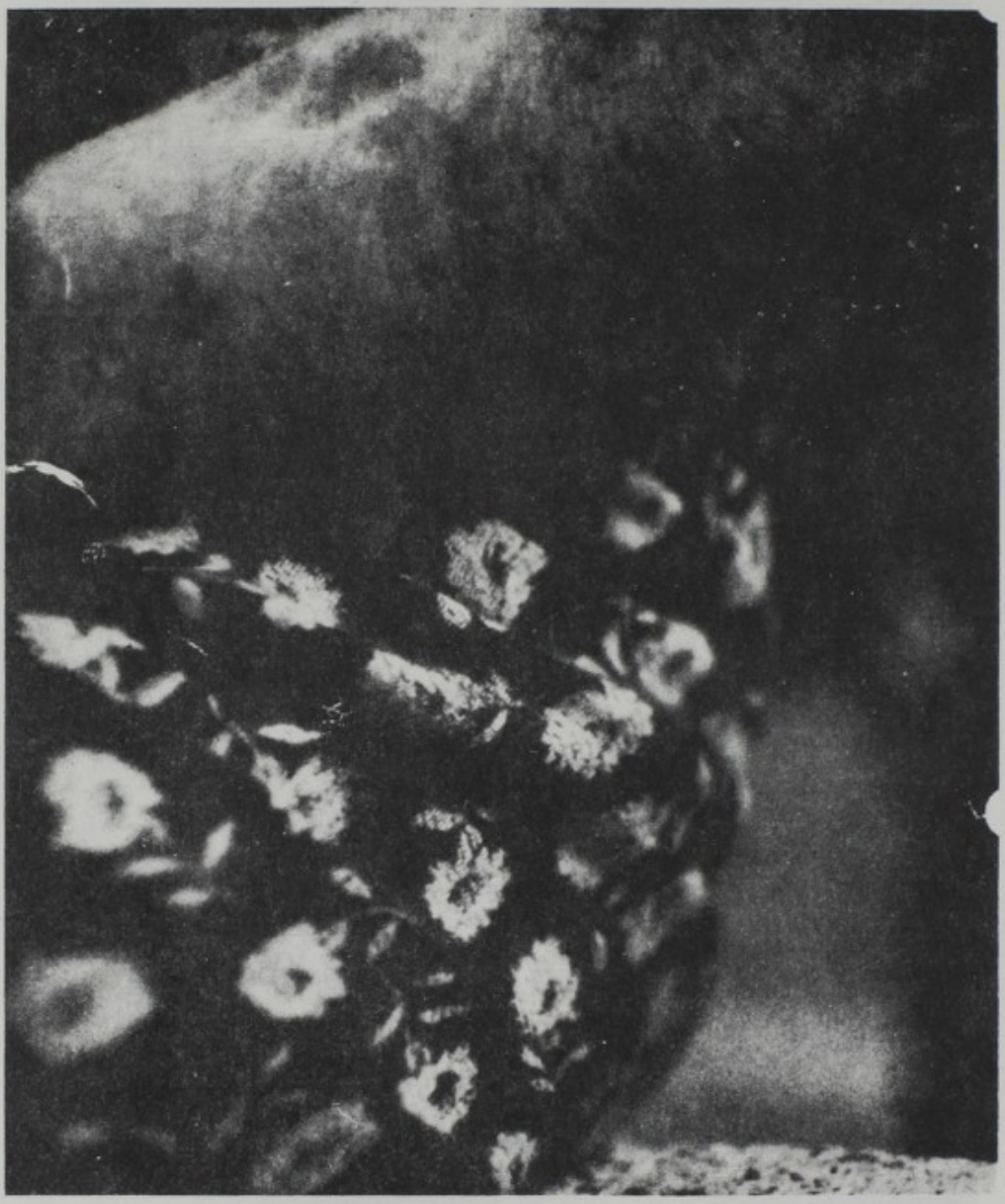


A TYPICAL MOON-CHILD

Figure 1

Sipu Hermana de Augustino of Ailigandi is typical of 152 albinistic Moon-Children recorded among the Caribe-Cuna Indians of San Blas Province of Lower Panama.

Journal of Heredity, Washington,
Vol. XLIV, No. 5, September-
October, 1953.



EXCESSIVE GROWTH OF HAIR

Figure 2

Moon-children bear straight, white down on the forearms and limbs which by the age of nine years may measure as much as 2½ cm. Fine hair is also present on the forehead and sides of the cheeks.

iameter. Benign tumorous growths have been seen on several Moon-children and skin cancer is not uncommon. The skin becomes much wrinkled by ten years of age, especially on the back of the neck, a condition which increases with age. The skin, from the age of about 1½ years, is covered with severe sores, due to infection of wounds, abrasions, and insect bites. The skin is rough and very dry. The lips exfoliate skin frequently, are enlarged and protrude. The tissues about the eyes often appear to be swollen.

At birth, head hair of the Moon-child is usually white, changing in some individuals through tow, to a rich golden in youth, and even to light brown, or even reddish brown in middle life. Some Moon-child hair is red in infancy. The head hair appeared finer because it seemed to blow about in the breeze more freely than pigmented hair. Micrometer caliper readings showed this to be the case for both males and females.

Although normal Cuna Indians are very smooth skinned, the Moon-children bear straight, white down on their bodies which on the forearms and limbs may measure from one-half cm. to 2½ cm. in length by the age of nine years. This amazing, fine hair was found on the appendages of all specimens examined. Fine hair is often present on the forehead and sides of the cheeks, and even on the ears of one Moon-child. Beard hair developing on three males is white.

The eyes tend to be of the oriental type in which the eyelids are invisible when the eye is open, whereas this kind of eye appears to be less common among normal Cuna.

Measurements of standing height were made for Moon-Children and controls of the same age and sex. Moon-children appear to be from about 2 to 7 cm. shorter than normal controls. Twenty-four Moon-child males average .3 kg. less than their controls which cannot be considered to have significance.

Head shape of Moon-children appears to be brachycephalic in a higher percentage than normal. No statistical data on this subject were collected, but in addition to my own observations the Indians themselves have remarked about this apparent correlation. The facial angle appears to be depressed by underdevelopment of the maxillary bone about the nose. They favor a Caucasian face shape.

Physiology

Specific gravity of the urine has been taken for a few Moon-child boys, and these are remarkably low. The specific gravities of the Moon-children average 1.006 whereas their controls averaged 1.015. In fact, these Moon-children show some of the lowest specific gravities ever recorded.

Through the courtesy of Dr. H. Heinmets, ultraviolet spectrum analysis was made on two samples each of urine from two Moon-child boys, (Placido and Galvis), taken in the morning and evening, each controlled by samples from two normal-skinned Cuna boys of comparable age. The results show that in these Moon-children some substance is greatly reduced in amount or absent entirely, having a peak at about 280 millimicra. This is the position at which the steroid estrogens are located and, hence, may indicate a paucity of male sex hormone. This type of abnormal curve is similar to one obtained from the urine of an albino negro boy.

Moon-children do not appear to have an incidence of tuberculosis above normal, but they almost constantly carry infections of the nose, head and throat. This fact may indicate that the general mechanism for producing antibodies is weak.

Readings were taken with the manual dynamometer on Moon-children and controls for both males and females. The hand strength of Moon-children, both males and females, is reduced.

The physical directors of four schools say that Moon-children, in general, lack endurance in physical contests. They seldom take part in athletic sports. They have a naturally slow gait and slow movements; because this lack of endurance is common knowledge, the town usually does not call upon them for heavy physical labor in community projects, and the house demands from them only the lightest of duties.

Moon-children, according to the observation of Dr. Luis Prieto, are slow in developing sexually. Among the Moon-child females, menstruation begins later than in the normal female, and the breasts are smaller in general. The breasts were very small on the 18-year-old Moon-child female that I was able to examine. Although they are usually fertile, Moon-child males are undersexed, and while tradition forbids them to marry, they never have been known to make advances or sex attacks as normal males would do under the restrictions of a rigid town government that makes prostitution practically impossible except in one or two of the some fifty Cuna towns. Indians have spoken to me regarding this lack of sex drive in Moon-child males which they say is one reason why brown Cuna girls do not want to marry them. This reduction in sex drive may be a correlate of the ultra-violet urinalysis picture for Moon-child boys mentioned above. The voices of Moon-children tend to be soft, and this is particularly noticeable in adult males—possibly another indication of sex-hormone deficiency.

Psychosomatic Behavior

The mentality of Moon-children appears to be normal, and no less than 14 of them have competed in formal school classes. It is a common belief among the Cuna that since they are unable to compete physically, they strive that much harder to succeed intellectually.

The chiefs of two large Cuna towns, Aili-



MOON-CHILD MOTHER AND HER MOON-CHILD DAUGHTER

Figure 3

This is the only case known in the whole Cuna tribe in which a Moon-child mother has given birth to a Moon-child.

gandi and Ustupo, as well as other residents, say that the Moon-children are stubborn and not tempered.

We have observed that Moon-children seldom smile, and when they do, it is usually quite feeble. Moon-children definitely lack facial expression.

It is noteworthy that Moon-children do not want to associate with each other, and at the ages of 12 or 13 (when the Moon-child girls find their normally pigmented friends marrying and having babies, and Moon-child boys realize that they cannot compete physically with other boys) they often cease to associate freely with normals and become somewhat non-social. They may, however, let loose at parties. This tendency appears to be due to their feeling of inferiority. However, notwithstanding this tendency to solitude, Moon-children may have a strong, personal determination to succeed. For example, one Moon-child girl of twenty years, who had not had a day of schooling previously, persisted through three weeks of night classes until she had learned phonetic reading better than those normals who had four weeks' training. A Moon-child boy of eleven years, finding that he could squeeze only eight kilos on the manual dynamometer, whereas his associates could squeeze twelve kilos, returned alone several times a day during four weeks, determined to better his record. Such persistence has allowed Moon-children to become leaders in their community in spite of their physical handicap. For example, Manauwikini and Maniotikinappi of Ailigandi are both medicine men of good reputation, and Manauwikini is official chica maker for several islands. Oliver of Ustupo knows the official six-day chant (absoket kantu) for exorcising community devils and is the appointed absoketi (exorciser) for Ustupo.

Heredity

Tracing Caribe-Cuna pedigrees is a difficult task due to lack of written records and the fact that many Cuna lack names. No calendar is kept, and the Cuna have had no written language of their own. Birth dates are not recorded. To speak of a dead person may hinder the chances of his soul getting to heaven. Thus, the collection of Cuna pedigrees becomes a matter of ingenious questioning and great diplomacy. From the pedigrees collected, we may draw definite conclusions concerning (1) the mode of inheritance and (2) the penetrance of the Moon-child gene in simplex.

Previously, the inheritance of the Moon-child variation was obscure, its occurrence being considered as due to the segregation of a Nordic blond gene in one instance, and in another it was thought to be sex-linked. The best study, that of Harris,[1] concluded indefinitely that it was a *recessive* of some sort and *due to one or more genes.* Many Cuna believe that the variation is the result of diet or maternal impressions caused by the mother-to-be or the father-to-be having gazed too frequently at the moon or some white object during pregnancy.

Recessive Inheritance

Ordinarily, Moon-children are forbidden to marry. However, old customs and codes have tended to break down recently, especially in Nargana, due to the impact of civilization from Colon and Panama City. As a result, several Moon-child women have married. Others have broken the chastity practiced by Moon-child women for centuries. These trends are so recent that previous observers (27 years ago) had not been able to find any offspring of Moon-children. Due to this trend, however, we were able to record that thirteen Moon-child women have borne twenty-five normally pigmented children in addition to one Moon-child girl.

Five Moon-child men have married, and all of them have families. The wife of one of these has given birth to two normally pigmented boys, but town gossips question their paternity. The other Moon-child men had a total of eight boys, and there seems to be no question as to their paternity. It is curious that boys only were produced, but this may be due to chance and does not affect our conclusions.

These data leave no doubt but that the Moon-child variation is a *recessive of some sort,* as Harris thought it to be, although Harris did not procure data that would decide of what sort.

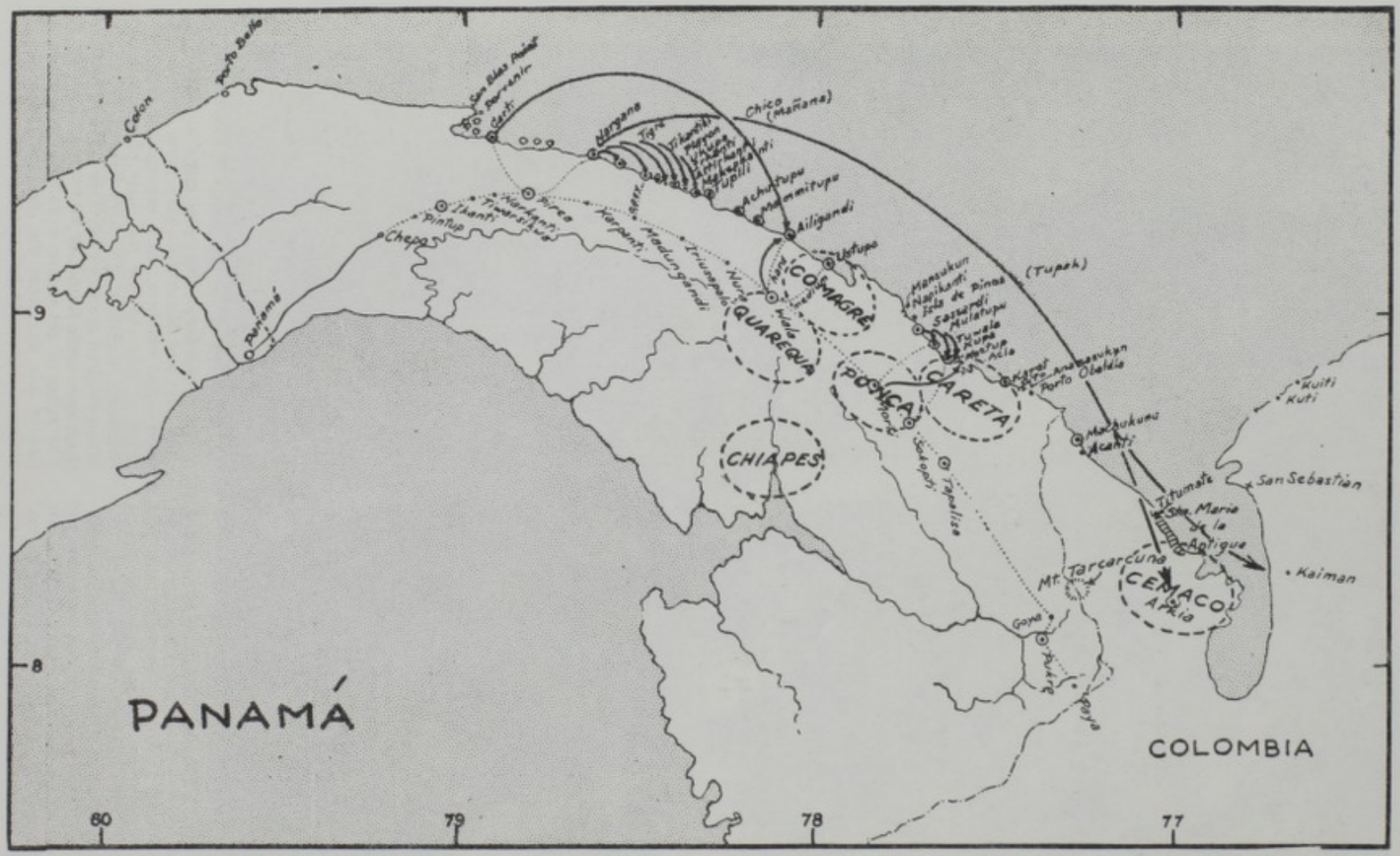
Autosomal Nature

Our data permit us to go further. We may ask, is it sex-linked or autosomal? We have data that are decisive for settling that point. Ten Moon-child women gave birth to a total of 14 boys, all with pigmented skin. This proves that the Moon-child gene complex is not sex-linked, and therefore must be autosomal, because the sons of Moon-child women would all be Moon-children if the condition were a sex-linked recessive.

Single Gene Substitution

Data from the pedigrees are sufficient to decide whether the Moon-child variation is due to one or two mutant loci. The matings of normal × normal in these pedigrees resulted in 285 children: 96 normal boys, 62 Moon-child boys, 72 normal girls, 52 Moon-child girls, and 3 normals of sex unknown.

These data demonstrate the fact that Moon-child boys and Moon-child girls occur in relatively equal numbers. In a segregating population of this size, on the basis of a single, recessive, mendelizing characteristic, 71.25 Moon-children are expected. One hundred and fourteen were found, or an excess of 42.75. The value of chi-square = 34.200 A deviation of this size from the ideal ratio due to chance alone would be expected in much less



LOCATION OF THE CARIBE-CUNA TOWNS **Figure 4**

Map of Panama showing most of the Cuna settlements. Arrows indicate the known migrations of the past fifty years. (Note: After the cut for the above map was made, it was discovered by the a[illegible] that the towns of Achutupu and Mammitupu lie between Ailigandi Ustupo, rather than between Ailigandi and Tupili as shown on the [illegible].p.)

1959 — raw: 50.526 % moon-children
1952 — raw 62.048 %

than one percent of similar samples. The deviation, however, is in the direction expected in collecting pedigree data for a simple recessive, due to emphasis on the Moon-children. Because of this disagreement with the expectancy, we must adjust the data to conform with a consideration of the Hardy-Weinberg law.

The expected proportion of recessives for each family size is obtained by use of the formula for the *a priori* method,* which is:

$$aa_n = \frac{1/4}{1-(3/4)^n}$$

where n = the number of children in the family.

No. children in family	Observed Normal	Albino	Calculated Normal	Albino
2	11	11	9.427	12.573
3	26	22	27.842	18.158
4	41	29	43.829	24.871
5	35	20	36.960	18.040
6	20	10	20.875	9.125
7	20	8	19.920	8.080
8	13	3	11.556	4.444
Total	166	103	170.409	95.291
Observed			166.000	103.000
Calculated from data			170.409	95.291
Expected deviation (d)			4.409	7.709
d^2			19.439	59.429
d^2/e			.117	.577

$x^2 = \Sigma\, d^2/e = .694$ $N' = 1$
P = between .30 and .50

Thus, the data agree closely with the expectancy on the basis of a simple, recessive character dependent upon a single gene substitution in duplex.

Other Variations in Pigmentation

Among the Cuna are found two other variations of lighter color than the average Indian but quite distinct from the Moon-child condition. Some have attributed these variations, as well as the Moon-children, to European admixture. In fact, all three variations appear to be confused in the minds of some who observe in them a graded series of pigment reductions from normal, through the lighter variations, and the several grades of Moon-child modification to extremely albinistic forms with white hair and clear blue, highly sensitive eyes. Harris apparently fell into this error.

The Indians recognize these shades, making a total of four in all, and Harris assigned genetic entities to each of them. The average Cuna Indian is a bit darker than R. R. Gates' skin color No. 4, but not so dark as his No. 3. The light Indian is about the shade of No. 6. The very light Indian is about the color of No. 7. The Moon-child is white or light pink as in No. 9. All of the Indians appear to have a little more yellow in their skin than the shades given in Gates' color chart.

Blonds

The Caribe-Cuna relate that about a century ago, three ship-wrecked European sailors (one named Sheppard) were adopted into the tribe. These married Cuna women and had children. Their children were not killed, as has been the customary fate of Cuna hybrids. There were observed at Ailigandi and Mammitupu several individuals of undisputed parentage of different families possessing very fair skin, lighter than or about the shade of Gates' color No. 7, with light hazel or greenish eyes. All these blonds have light hair but with none of the reddish brown that is often present in Moon-child hair. At Achutupu several members of one family have light hair, very fair skin and gray eyes. It appears definite that these segregations are not due to recent hybridization, but they may have resulted as recombinations from crossing with blond Europeans during earlier times, and possibly they are descendants of the sailors mentioned above. Moon-children have not occurred in these particular families, and so it appears safe to conclude that these persons represent blond types comparable with those of Europeans rather than heterozygosity for the Moon-child variation.

Heterozygosity for the Moon-Child Gene

When we examine normal individuals in Moon-child pedigrees, we find that these families may also contain persons of fairer complexion than that of the average Indian, although not so light as the light-haired blonds that we have just described. These are about the shade of Gates' color No. 6 or lighter. There tends to be a yellowish cast to the complexion of these persons, and they have dark eyes and black hair.

What evidence do we have to support the idea that heterozygotes for the Moon-child variations are likely to be lighter in color than the normal Cuna Indian, especially in females?

An examination of three groups of individuals can shed light upon this problem, namely:

1. sibships that include albinos
2. the parents of albinos
3. the children of albinos

Certain pedigrees are given in Figure 5 in which shade of pigmentation has been determined for most of the individuals represented. Matings 1:1, 2; 1:2, 3; 1:4, 5; 2:7, 8; 2:22, 23; 3:7, 8; 5:1, 2; 5:14, 15; 6:8, 9; 6:14, 15; 7:1, 2; 7:11, 12; 8:9, 10, produced a total of 17 normal males, 4 normal females, 12 light males, 12 light females, 12 Moon-child males, 10 Moon-child females. It will be seen that there is a paucity of females (29 pigmented males; 16 pigmented females) where equality of numbers is expected. However, of the pigmented males, 17 are normal and 12 are light. Of the females, 4 are normal and 12 light. Thus,

*I am grateful to Professor David C. Rife for checking these calculations.

there appears to be a tendency toward normal males and light females.

Two-thirds of the pigmented males (that is, 19.14) are expected to be heterozygotes. But only 12 are light, suggesting that not all heterozygotes are light.

If we examine the parents of albinos, we are dealing with a population of individuals all of whom are heterozygous. Individuals 1:1, 2, 4, 5; 2:7, 8, 22, 23; 3:9, 10; 5:1, 2, 3; 5:14, 15; 6:14, 15 are thus, all heterozygotes. Of these there are four that are classed as normally pigmented males, no normal females, five light males and eight light females. Here we see that all of the heterozygous females are light and that more heterozygous males are light than normally pigmented.

It is true that the children of albinos are notoriously light complexioned. Such pigmented children are all heterozygotes. We have examined the children of a number of these albino parents.

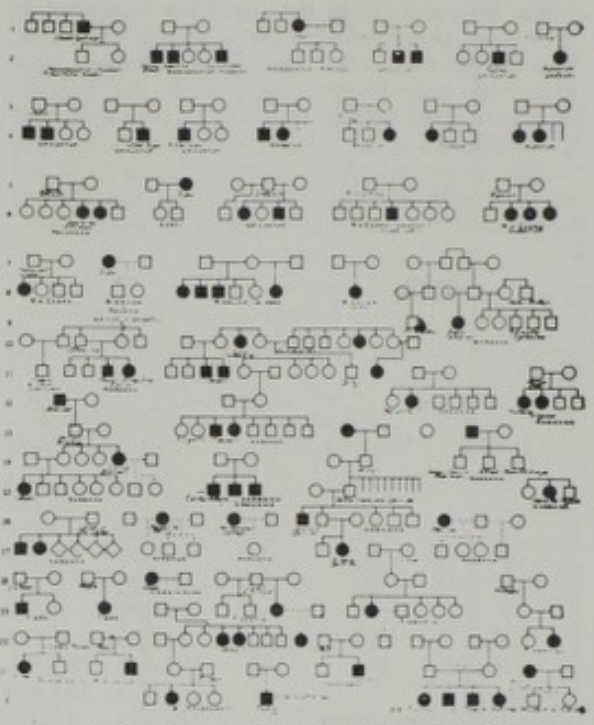
I have recorded the shade of the children of nine albinos. Their children may be classified as: 1 normally pigmented boy, 5 light boys, and 4 light girls.

These three lines of evidence all indicate the same phenomenon, namely, that individuals heterozygous for the Moon-child gene tend to be lighter in pigmentation than are normal Indians. Practically all heterozygous females would appear to be light, whereas a certain percentage of heterozygous males will be classified by investigators as of normal Indian pigmentation.

Several explanations for the darker exceptional males are possible. Time spent in the sun may account for a good portion of it, and yet we must not overlook the possibility of other factors. For example, slight hereditary diluations in pigmentation which of themselves are insignificant, may provide a background on which the albino gene in simplex may produce noticeable effects. Such coöperative effects are known in mice and rats. If the gene producing the insignificant variation and that producing the Moon-child variation happened to be allelic, such a lightening of the heterozygote would be very likely to occur, as seen in the albino alleles of mice and rabbits.

Certain pigmented individuals in three pedigrees (not shown in Figure 5) are recorded as being of this fair-skinned type. Examination of a fourth pedigree shows that normal, fair-skinned and Moon-children may be born to the same couples. Again, it was noted that often the parents of Moon-children are fair-skinned. Thus, we are led to suspect that the dark-haired, fair-skinned individuals occurring in Moon-child families represent the Moon-child gene in simplex—but that its blond penetrance in simplex is something less than 100 percent.

Tines Ismit, a little boy of Ailigandi, was definitely a Moon-child with nystagmatic eyes, but his skin took on a sallow tan and he showed less of the other tendencies characteristic of Moon-children. Investigation of his family revealed that his condition was probably due to a combination between the blond gene present at Achutupu and the Moon-child gene.



PEDIGREES OF THE MOON-CHILD CONDITION

Figure 5

Inheritance of the Moon-child Condition. Squares represent males, circles represent females, shaded symbols represent Moon-children. Dash lines represent illegitimacy.

One red-headed woman with dark eyes was found on Ustupo, but whether this gene is of European origin or represents a local mutation, it is impossible to say.

The appearance of the Moon-child variation in nearly all island villages of the Cuna today suggests that the mutant gene was widely distributed in the germplasm of the tribe before the dispersal of these groups—because there is little intermarriage between villages, and each village tends to inbreed.

Migrations of the Moon-Child Gene

It is known that during the seventeenth century the San Blas islands were as yet unoccupied. During buccaneering days the Indians aided the pirates against the Spaniards. Following this, Cuna migration gradually took place from the mountains to the shore and out upon the islands.

In order to study the problem of Moon-child gene migration, Indian visitors from the hostile mountain villages were questioned carefully about the occurrence of Moon-children in their villages. The results show that Moon-children are known to have appeared in

Ikanti, Pirea, Wala, Morti, Sokopti, and Tapalisa, while Marsh reported seeing a number of albinos back of Pukro. These are towns scattered all along the Cuna trail on top of the Cordillera of San Blas, as will be seen from the tentative map that I have constructed.

Further inquiry revealed that there are at least seven commonly used trails leading from the mountain villages to the coast, by which Mountain Indians come down to visit relatives who migrated there years ago.

Carti and Nargana, both towns segregating Moon-children, are connected by trails with Narkanti and Pirea in the mountains in which latter town Moon-children have occurred.

An "easy" trail connects Tikantiki with Madunkanti in the mountains. Tikantiki has Moon-children. This is undoubtedly the trail used by Wafer, and he reported Moon-children in the mountains in the 17th century.

Ailigandi and Ustupo both have many Moon-children. Both these coastal island towns are connected by trails with Wala, a mountain town that has produced Moon-children. As a matter of fact, it is known that Ailigandi was founded by people from Carti and from Wala, and hence the Moon-child gene probably came into this town by two routes.

A trail leads from Morti in the mountains to Sassarti and Mulatupu which are close together. Both Morti and the extinct town of Sassarti have had Moon-children. Morti and Carti people founded Koetup.

With the migration of the Cuna from these mountain villages to the coast the Moon-child gene came with them.

The inhabitants of some islands "cannot remember" from whence they came. (This may mean that they do not care to tell.) However, for certain other island towns, not mentioned above, the migration routes along the coast are known.

Because of the deadly malaria at the coastal town of Sassarti, the Indians moved out to the islands of Mulatupu, Tuwala, and Kupa. Moon-children from this source are found on Mulatupu and Tuwala.

The most extensive migrations took place when Padre Gasso founded his Catholic mission at Nargana in 1907. Many Indians from Nargana fled from the "horrors" of Christianity and civilization, founding the towns of Tigre, Ukupa, Irkanti, Itirrkanti. Individual families took refuge in various already established towns that would receive them along the coast. Some refugees went as far as Arkia, Kuti, Kuiti, and Kaiman. Tigre, Makepkanti, and Arkia have Moon-children, as a result of this migration.

Again, in 1924, during the Revolution, another migration took place although it was not as extensive as the 1907 shift of population.

I do not know from whence the inhabitants of Karet and Machukuna came, but they are well within the area with which Balboa's Spanish colonists of Santa Maria de la Antigua were acquainted. Both these towns have Moon-children, although it is my opinion that the towns probably were founded in relatively recent times.

It would appear, then, that the facts favor an ancient origin, rather than a recent one. Possibly the mutation occurred in the Cuna stock that moved northwest from the Tarcarcuna mountain region of tribal origin shortly after that migration started. However, this possibility can only be tested by exploration into the several Cuna towns still existing in the high mountains of Darién, a region still dangerous for the lone white man to enter, and yet reports say that albinos are present in the mountains of Darién.

A plausible explanation of the time of origin of the Moon-child variation appears to be that of a mutation in pre-Cuna days. The native missionary, Alcibiades Iglesias, has visited among various North American tribes and of them all, he feels that the Winnebegos and Navajos most closely resemble his people, although these tribes appear to be of mixed origin. While among the Navajos he felt as if he were among the Cuna, his own people. Again, the Cuna claim to be related to Aztecs and Mayas. Curiously enough, albinism is found among the Aztecs and Navajos, and I have not been able to obtain records of Winnebegos and Maya.

If these peoples are related as they appear to be (although of mixed origin) and if albinism (the Moon-child variation) is present among several of these tribes, then it appears likely that a pre-tribal mutation to the albino-producing form occurred in the pigment gene of one of the migrating stocks that gave rise to these several tribes.

In that connection it is interesting to note that the Chocos Indians whose territory has bordered upon that of the Cuna since earliest times have never been known to have produced a Moon-child.

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XXXIX

ALBINISM, XERODERMA PIGMENTOSUM, AND SKIN CANCER[1,2]

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SUMMARY

Albinism and xeroderma pigmentosum are similar in that both groups of patients have dry skins, irritated eyes, large freckles, keratotic spots, and skin ulcerations brought about as a response to light. Both conditions are inherited as simple, recessive entities. Under certain conditions, both develop skin cancers. They differ in that hair and eye pigment in xeroderma is normal, but greatly deficient in albinos, resulting in nystagmus. Xeroderma has a lower threshold of sensitivity than has albinism, often developing many malignancies by 6 years of age in the temperate zone, whereas Caucasian albinos in the temperate zone seldom develop cancers. Cuna albino Indians in the tropics, however, often form skin cancers in their late teens or early twenties and all show actinic keratoses at the age of 3. Xeroderma is quite rare, possibly having an incidence on the order of 1 in 20,000; albinism occurs about once in 10,000. Among the Navajos it appears twice in 10,000 and, Cunas have 45 albinos in 10,000. The gene for xeroderma pigmentosum may be partially sex-linked, whereas, that for albinism is autosomal. The malignancies of xeroderma are usually basal-cell and squamous-cell carcinomas; melanocarcinoma also occurs; albino skin cancers among the Cunas are almost always squamous-cell carcinomas. The heterozygotes of xeroderma pigmentosum may be freckled; those of the albino are not freckled but may be intermediate in skin color between albinism and normal pigmentation in both Caucasians and Amerindians. Cuna albinos (Moon-children) present an extensive syndrome of pleiotropic effects that can be recognized in nystagmus, decreased body length and weight, a weak hand squeeze, lack of sweating and low specific gravity, fine head hair, growth of hair on appendages, lack of energy, deficient male sex hormones, and stubborn temperament, in addition to their propensity to develop skin cancers.—NCI Monogr. No. 10: 349–359, 1963.

ALBINISM and xeroderma pigmentosum have been linked together for discussion on this program because they have a number of clinical signs in common: light-sensitive, dry skin, photophobia, freckles, keratotic

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[3] The author wishes to thank V. C. Vaughn III, M.D., and H. J. Peters, M.D., for sections of xeroderma pigmentosum provided for this paper. He is also grateful to Archibald McFadden, M.D., for sections of skin biopsy material collected from Cuna Moon-child albinos by Rowland Icke, M.D., as well as for permission to quote.

patches, and a tendency to form skin cancers. However, these two entities differ in many respects, as we shall note here.

XERODERMA PIGMENTOSUM

This condition is described as a precancerous disease of the skin usually first manifested in childhood. It is characterized by large freckles, atrophic areas, and keratotic spots (fig. 1).

The first signs of xeroderma pigmentosum in childhood may be a crowded distribution of enormous freckles on all exposed areas, dry skin with dandruff, and, especially, irritation of the conjunctiva. Soon keratoses, warty excrescences, and ulcerations appear. These signs are quickly followed by the profuse development of malignancies. Hair and eye pigmentation are normal in this disease, and there are no congenitally associated eye defects. Because irritation of the eyes produces the initial discomfort, the xeroderma pigmentosum patient may be brought first to the Ophthalmological Clinic where the preclinical signs of cancer are not likely to be recognized.

Histology

Atrophy, acanthosis, and hyperkeratosis are seen in histological preparations together with deposits of melanin in the basal layer, the lowest layers of the stratum spinosum, and chromatophores of the upper epidermis. Areas of the epidermis may resemble lentigo malignum or junctional nevus. Basal-cell, squamous-cell, or melanocarcinoma may complicate the picture of xeroderma pigmentosum (fig. 3).

There is basophilic degeneration of the collagen with atrophy in the dermis. The elastic fibers are also degenerated. Neoplastic elements are usually basal-cell or squamous-cell carcinomas, although spindle-cell carcinomas do occur.

Treatment

The usual treatment for xeroderma pigmentosum is electrocautery or surgical removal of the malignancies as they appear. I have known a case in which a hospital staff did not recognize this rare syndrome and carried out a series of intensive X-ray treatments that probably aggravated the condition, although I have found radiation recommended in a pathology text.

Prognosis

At present, there is no cure for xeroderma pigmentosum, and the skin malignancies increase rapidly in number, in spite of treatment, until metastases finally spread to the internal organs and cause death.

Heredity

Xeroderma pigmentosum is familial, that is, a recessive disease. Being quite rare, it occurs due to consanguinity much more often that to random

mating. Both Fisher (*1*) and Haldane (*2*) agree that there is mathematically sound evidence for assigning the recessive casual gene for this disease to the homologous portion of the X and Y chromosomes, because of partial sex linkage. However, their maps do not agree in the finer details of linear order of genes or the number of units that separate them. The partially sex-linked associates include the genes for achromatopsia and congenital night blindness. On the basis of this work, chromosome maps, for the homologous portions of the X and Y chromosomes of man, have appeared in textbooks for more than a decade and locate the zeroderma gene and others in this region. Recently, however, Morton (*3*) has criticized this mathematical treatment, declaring that the results obtained are merely the effect of a cryptic statistical error created by an improper selection of data.

Heterozygotes for xeroderma pigmentosum frequently exhibit freckled, sensitive skins, but do not develop the disease. The condition probably occurs less than once in 20,000.

Figure 1 shows a case of xeroderma pigmentosum that I first recognized at the Massachusetts General Hospital in its preclinical stages when dry skin, freckles, and dandruff were the only signs of the disease. Conjunctival irritation had begun, but was so slight that it might have been caused by rubbing the eyes while crying or by a slight allergy. A year and a half later, at the time of the photograph, five cancers had been removed from the cornea, cheek, and back of the neck.

ALBINISM

In contrast to xeroderma pigmentosum, albinism is recognizable by snow-white hair and a great reduction in ocular pigmentation producing the nystagmus so characteristic of this disease. The exposed, light-sensitive skin takes on a characteristic pink color, softened by its white lanugo. There is some suggestion of reduced metabolism. In the temperate zone, and with no undue exposure to sunlight, these patients do very well. Because of their ocular difficulties, albinos are frequently found in schools for the blind.

Treatment

In the temperate zone there is no treatment recommended for the disease aside from protective glasses, protective clothing, and staying out of the sunshine.

Prognosis

The prognosis for albinism in the temperate zone is excellent, and it is seldom thought of as a disease but rather as the sensitive skin accompaning an eye defect. Skin cancer rarely occurs in these albinos, if the precautions mentioned are taken.

Heredity

True albinism in man, as in all mammals, is a simple recessive, mendelian characteristic dependent on the presence of a single pair of genes. In forms such as the mouse, rat, rabbit, and cat, these genes are members of a series of multiple alleles or alternative forms of the same gene molecule. Other members of the series include chinchilla and himalayan. There is some evidence that at least one other member of the series may exist in man, characterized by pink eyes and some pigmentation in the hair, but the evidence is not conclusive.

The frequency in Europeans is estimated at about 1 per 10,000. In blonds of the Caucasian race, heterozygous for albinism, the eyes may be sensitive and the hair color lighter than that of true blonds in the family not carrying the albino gene. In like fashion, mice greatly diluted in coat pigmentation will often be even lighter in fur color when they carry the albino gene heterozygously.

Thus far, we have described the conditions for Caucasians having albinism in the temperate zone. However, for Caucasians and even for darker races in the tropics, albinism may have a very severe, cancerous import due to the actinic rays of the blazing sun.

Caribe Cuna Moon-Child Albinos

For 13 years I have been in touch with the primitive Caribe Cuna Indians of San Blas, who live mainly on the string of offshore atolls that skirt the Caribbean coast of Lower Panama. I have visited them 8 times. Here we find the highest incidence of albinism in the world, now numbering about 45 per 10,000. Less than 95 individual albinos, called Moon-children by the natives, are available for study today. I say "less than 95" because the number I first counted seems to be decreasing—partly due to infanticide of the newborn.

Among the Cunas, albinism shows several characteristics not noted generally in Caucasian albinos of the temperate zone (fig. 2). Fine, white hair, sometimes an inch and a half long, grows on the lower arms and limbs of Cuna albinos, whereas the skin of the brown Indian is completely devoid of body hair. Head hair is finer in diameter than normal hair. Short, fine, white hair frequently grows on the sides of the face and even on the rim of the ears. Hard, keratotic spots are mingled among large freckles, and the skin presents a dry, senile appearance. It becomes thickened with wrinkles on the back of the neck at a very early age and is greatly thickened on the backs of adult males. Cuna albinos do not sweat. They are slightly shorter and lighter in weight than are brown-skinned Indians (*4*).

San Blas albinos lack energy and cease to be active in athletics by 13 or 14 years of age, taking over the job of referee or manager of the team. When children, they constantly carry infections of the nose and throat and appear to be deficient in the building of antibodies. On the skin of Cuna albinos mosquito bites become infected. The albinos seem to lack

energy and have a low metabolic level. The power of the hand squeeze is reduced. The male sex drive is low in albinos and they seldom marry. The voice is high-pitched in males as though deficient in male sex hormones, and ultraviolet spectrum analysis of the urine reveals almost complete absence of the steroid estrogen peak in several teen-aged albino boys examined. However, Cuna Moon-child females are fertile although they mature late (*5*).

The weakness of albinos is rather general among mammals (*6*). Because of this weakness Cuna Moon-child albinos occupy a peculiar position in tribal society (*7*). The town council calls upon them for less rigorous physical labor than exacted from brown-skinned Indians.

It requires a certain amount of basal metabolism to commit crimes. Sex offenses are highly taboo, and until recently the offending parties were killed as well as the resultant bastard child. Albinos are said to sin less, in these respects, than other persons and, therefore, to be on better terms with Tiolele the Sun god. Because of this better behavior on earth, Moon-children will receive better houses in heaven, and others will not be permitted even to look into their heavenly mansions unless they have made friends with 8 Moon-children on earth. At the time of eclipse only the albinos are holy enough to rush out with bows and arrows to shoot and kill Achusimmutupalit, the Earthmother's Placental Monster, who is trying to end the world by swallowing up the sun or moon (*8*).

On the other hand, because of the weakness, suffering, social handicap, and early death, infanticide of the newborn has always reduced the Moon-child incidence in the Cuna population (*8*). The incidence was at its height a decade ago due to the influence of the great chief Nele Kantule, who said: "Because the Moon-children are on better terms with God, let us keep the Moon-children that they may tell us more about God." However, since the death of Nele Kantule, the incidence of Moon-children has declined, and although I have been told of 4 cases of infanticide of newborn albinos, usually the information never gets beyond the 3 old midwives who quickly bury the infant in the sand beneath the mother's hammock.

Albinism among the Cunas is inherited as a simple, recessive characteristic in our 1960 pedigree data. The percentage of albinos far exceeds 25 but, when adjusted to account for the Hardy-Weinberg considerations, these data fit very well with the expectancy, as shown in table 1.

At 1 degree of freedom in a chi-square table, a χ^2 of 0.870 indicates that the probability is between 0.30 and 0.50. This means that as great a deviation from the expectancy as present in our data would be expected due to chance alone in between 30 and 50 percent of all samples of the same magnitude. It would fit better were it not for infanticide.

Thus, our data on the inheritance of the Moon-child variation fit well with a mendelian 3:1 ratio. Hence we can say that the Moon-child variation is a simple, recessive mendelian characteristic dependent on one pair of mutant genes.

Heterozygotes are usually lighter in color than normal brown skins, and since this lighter color is preferred in this tribe there is actually a

TABLE 1.—Cuna Moon-child (albino) inheritance. Statistics to account for the Hardy-Weinberg law: 1960 field data

Number in sibship	Calculated percent of recessives (aa)*	Total No. of children	Calculated No.		Observed No.	
			Moon-children	Normal children	Moon-children	Normal children
2	57. 1428	22	12. 571	9. 429	15	7
3	43. 2432	48	20. 757	27. 243	18	30
4	36. 5714	64	23. 406	40. 494	18	46
5	32. 7784	75	24. 584	50. 416	20	55
6	30. 4128	30	9. 124	20. 876	11	19
7	28. 8512	14	4. 039	9. 961	4	10
8	27. 7813	24	6. 667	17. 333	9	15
9	27. 0295	9	2. 433	6. 567	1	8
Total		286	103. 581	182. 419	96	190

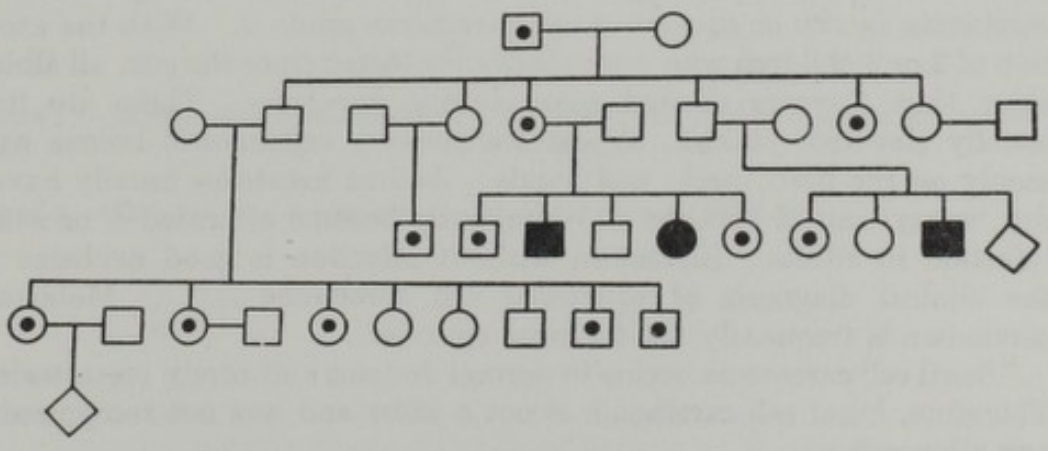
*The proportion of recessives (aa) is $\frac{0.25}{1-(0.75)^n}$ where n is the number of children in the sibship. Chi squared = sum of $\left[\frac{\text{deviations (observed} - \text{calculated)}}{\text{calculated number}}\right]^2 = \frac{57.471561}{103.581} + \frac{57.471561}{182.419} = 0.870$ with 1 degree of freedom $P = 0.30-0.50$.

social selection for heterozygote to marry heterozygote, guaranteeing the production of more albinos than would occur on the basis of purely random matings (text-fig. 1).

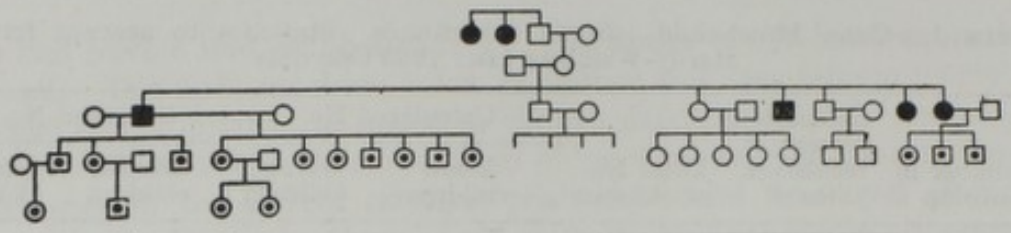
Heterozygotes for albinism were also lighter-skinned than the average among the Navajos (text-fig.2).

Although to speak of the dead is taboo in San Blas and to hide a lesion when one has it is customary, a number of years ago I began to realize that many of the Cuna albinos had open cancerous lesions on the cheek, eyelids, nose, lip, or arm in their teens and twenties. Further investigation revealed that metastases of skin cancer are probably the chief cause of death in albinos that live to grow up.

By inquiring quietly of educated Indians about these lesions of the Moon-children, I learned that a skin lesion became extensive, ran a clear exudate, and excavated inwardly. The patient took to his hammock, his arms and legs became emaciated, and after a number of months he



TEXT-FIGURE 1.—Pedigree of albinism among the Cuna Indians. *Squares* represent males; *circles*, females; *blackened symbols*, albinos; symbols bearing a *central spot*, light-brown-skinned individuals; *unshaded symbols*, normal dark-brown Indians.



TEXT-FIGURE 2.—Pedigree of albinism among the Navajo Indians. Symbols the same as in text-figure 1.

died. As the years passed, more educated Indians were willing to supply information. During the past year I have been advised of 5 deaths from skin cancer among Cuna albinos, and there were probably others.

The first biopsy specimen listed was examined by J. K. Sass, M.D., and the rest by A. W. McFadden, M.D. I have known personally for 12 years all 5 of the albino patients biopsied (fig. 4).

1) Pedro Arvila (albino Indian), 34 years—squamous-cell carcinoma had been removed from cheek: ulceration; temple. *Actinic keratosis.*
2) Galves Beker (albino Indian) 18 years: brownish-red papule; abdomen. *Solar elastosis.*
3) Ladislao Ismit (albino Indian) 10 years: brownish papule, slightly elevated; right forearm. *Verruca.*
4) Kawinti (brown Indian) 50 years: small ulcerated papule; suborbital. *Basal-cell carcinoma.*
5) Edna Perez (albino Indian girl) 14 years: dark-brown macule; right lateral forearm. *1. Ephelis. 2. Solar elastosis and hyperkeratosis.*
6) Placido Miseli (albino Indian) 24 years: papule; left subcostal. Slightly friable, rapid growth. *Elevated basal-cell carcinoma having a trabecular and a cystic pattern with the presence of mucous material occupying the cystic spaces.*

Recently, Dr. Archibald McFadden visited San Blas and has sent me a confirming account of his observations on the skin cancer of Cuna Moon-children that should be included here because of its brevity and completeness:

"All the skin cancer in the Cuna albinos is squamous cell (syn. prickle cell, epidermoid). The incidence of premalignant actinic (senile) keratoses in albinos is extremely high. These may be considered squamous cell carcinoma *in situ* or squamous cell carcinoma grade ½. With the exception of 2 or 3 children who were always protected from the sun, all albinos older than 3 years showed some actinic keratoses. These are firm, usually elevated, pinkish, almost translucent, asymmetric lesions commonly on the head, neck, and hands. Actinic keratoses usually have a dry 'warty' cap of keratin, and frequently become ulcerated $\bar{c}$/ or $\bar{s}$ mdg infection in adults. Ulceration without infection is good evidence for the clinical diagnosis of squamous cell carcinoma . . . . Metastatic carcinoma is frequently the terminal episode.

"Basal cell carcinoma occurs in normal Indians and rarely metastasizes. Therefore, basal cell carcinoma is not a killer and was not recognized in any albinos."

It should be stated that after this account was written, a basal-cell carcinoma was diagnosed in Cuna albino No. 6, Placido Miseli.

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Linkage studies on albinism have revealed no associations, but if albinism is allelomorphic to red hair, as thought by Wright (*9*), it may someday be found linked to the A-B blood group series.

The incidence of albinism among Navajos is about 2 per 10,000; compared to that for Cunas (Moon-children), about 45 per 10,000; and for Europeans 1 per 10,000, as mentioned.

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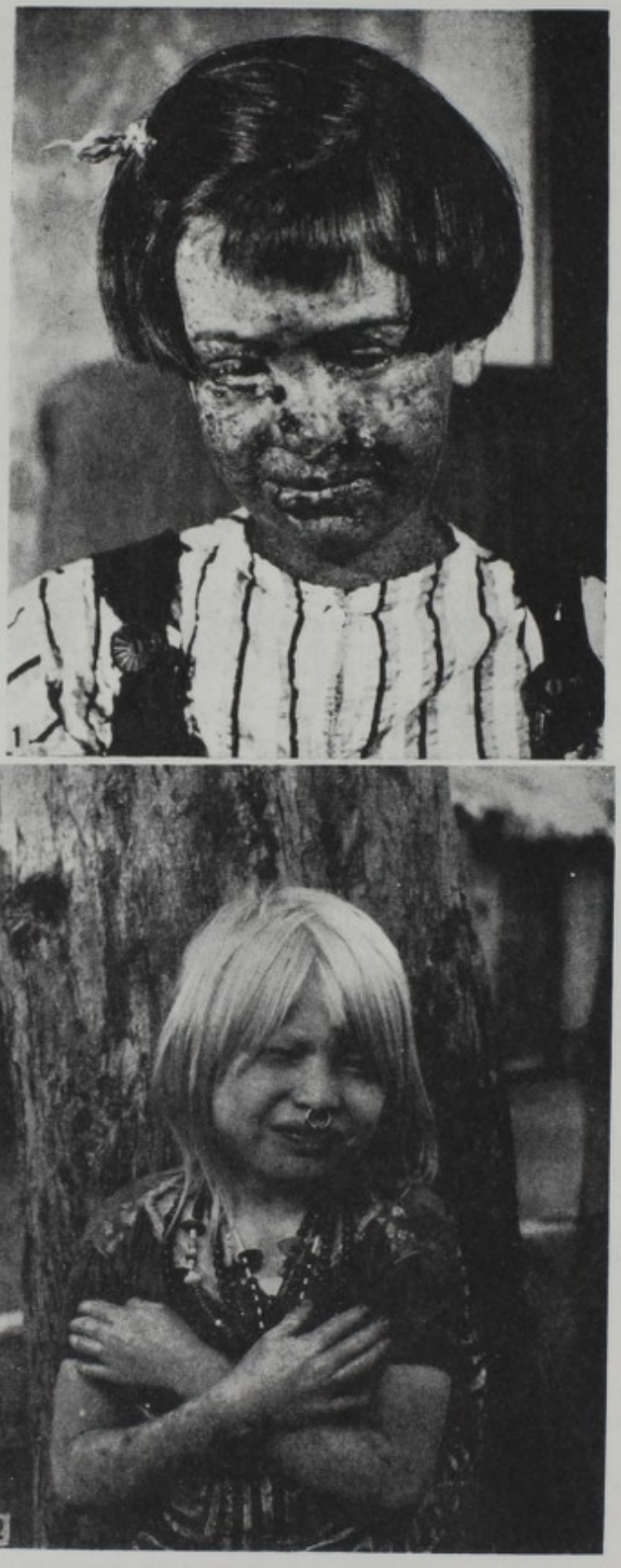
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Plate 36

Figure 1.—Xeroderma pigmentosum in a 7-year-old girl of French Canadian extraction.

Figure 2.—Albinism in a 5-year-old Caribe Cuna (Moon-child) girl.



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PLATE 37

FIGURE 3. Section of xeroderma pigmentosum skin cancer. *Note* keratin plug, patchy parakeratosis with nuclei visible in the corneal layer, perivascular infiltration, thinning of the malpighian layer as well as irregular elongation of the rete ridges.

FIGURE 4. Section of an albino (Moon-child) skin cancer. No. 6, Pacido Miseli. *Left end of section*, basal-cell carcinoma; remainder, normal tissue.





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Pigment Gene Pleiotropy in The Cuna Indian Moon-Child*

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Introduction

In 1941 I showed that the melanotic form of the wild gray Norway rat, as well as the piebald condition, and albinism are not isolated genetic entities, but rather each is the external indicator of a unique syndrome of modifications of glands, sense organs and brain [1] determining specific alterations in physiology that, in turn, modify behavior.[2] If these three coat color genes are all present in the same individual, their pleiotropic modifications are additive and largely account for all the physical, physiological and behavior modifications found in the tame Wistar albino rat.[3] The summated physical and physiological effects of these three coat color genes plus the effects of any other unlabeled taming genes that have mutated in the Wistar or related tame stocks and have become homozygous constitute the "marks of domestication" written about by Darwin, and identified anatomically, physiologically or behavioristically in

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the tame Wistar albino rat by such investigators as H. H. Donaldson,[4] J. C. Donaldson,[5] Keeler and King [3], Rogers and Richter [6], Fish and Richter,[7] Griffiths,[8] Richter,[9] Stone,[10] Hall,[11] Farris, and Yeakel [12] and others.

All these researchers except Keeler and King had the disadvantage of not knowing how many unidentifiable genes making for physical modification, and thereby for greater tameness, had mutated in their tame stocks that reduced the wild manifestations of their gray coat color animals in the F_2 and the Norway-Wistar hybrids backcrossed to their Wistar parents. Keeler and King studied not only the F_2 of a Norway-Wistar cross but they also investigated the coat color mutants that cropped out after the 12th generation of captive gray Norways, these having the advantage that their results are clear cut and not weakened by the presence of unlabeled taming genes present in the tame albino stocks studied by the other investigators.

The studies of Keeler 1943, 1945, 1946, 1948 and his coworkers have shown that these mutant coat color genes themselves are the causes of whole syndromes of unique pleiotropic modification of glands, sense organs and brain. The study of pigment gene pleiotropy has been extended from rats to mink and to foxes. It has been explored slightly in man both in albinos and in red heads, where it finds medical application.

Because of the implications for psychology, psychiatry and medicine it was decided to study as many as possible of the 144 Cuna Indian Moon Children that I registered in San Blas Province, Panama, under the assumption that the Moon Children represent an albinistic syndrome like the coat color syndromes of rats, mink and foxes and not just a lack of pigment. The fact that the Moon-Children are all from the same small tribe of 23,000 persons, gives the advantage of uniformity of residual hereditary background, upon which the characteristics of the syndrome will stand out more sharply than in albinos culled from heterogeneous stocks, as would be the case if we studied albinos in the United States.

We are particularly interested in problems of Mental Retardation, as well as the psychological and psychiatric aspects of these studies. We are interested in any deviations in morphology and physiology, especially those that might contribute to changes in behavior. It is common belief that albinos tend to be mentally retarded, but there are brilliant exceptions presenting a problem that we would like to elucidate. We are concerned with producing a detailed description of the Moon-Child Syndrome.

A large team of specialists cooperated in this research program; Major Donald Moyer, M.C., U.S.A., Dermatologist; Joseph Bohorfoush, M.D. Cardiologist, Haematologist; Serio Alvarez-Mena, M.D., Cardiologist; Reichart Johnson, D.D.S., Dentist; George Courtney, Optometrist; Horace Stewart, Ph.D., Psychologist; Mrs. Virginia Balbona, M.A., Intern in Psychology; Helen Pessino, M.D., Radiologist; Mr. Walter Bowman, Technical Laboratory Director; Lillas James, M.D., Asst. Medical Geneticist; Julian Gomez, M.D., Psychiatrist; Hosea Balbona, M.D., Psychiatrist; Jose G. Men-

dosa, M.D., Psychiatrist; Joaquin Piedra, M.D., Psychiatrist; Carlos Maruri, M.D., Psychiatrist; Mr. Herbert Goldsmith, Music Therapist; Miss Becky Fuller, Laboratory Assistant; Miss Penny Edwards, Tissue Culturist; Virendra Mahesh, Ph.D., Biochemist; Herman Dominguez, M.D. Tissue Culturist; and Jose Rauco, M.D. Otolaryngologist.

Examinations

After cursory examination of 35 Moon-Child albinos on the San Blas Coast by Drs. Moyer and Keeler, six albino boys ranging in age from 21 to 36 years of age together with paired brown skin controls of the same age and sex were brought to the Milledgeville State Hospital for two weeks of intensive study. Each member of the above named team was responsible for the examinations in his own specialty. Findings of interest that they obtained will be reported here.

Anthropometics

Measurements were recorded for weight, height, chest circumference inhale and exhale, wrist circumference, length of tibia, length of femur plus tibia, metacarpal dimensions, head circumference, parietal diameter of head, fronto-occipital diameter of head, facial length, nasal length, manuometer deflections. The results showed the overall body size of the albinos to be smaller than that of the controls rather than to be changed in bodily proportions. However, the greater mean length of the albino nose becomes statistically significant when it is expressed as a function of facial length, indicating that the albino nose is, in contrast, proportionately longer than the brown-skinned one, and the figures for the third metacarpal indicate that the albino shaft is proportionately narrower.

It is interesting that mutant albino mink, rats and other mammals are smaller than normals and in rats the amount of reduction in body weight and body length are almost identical with the reduction in Moon-Children.

Moon-Child Skeleton

The bones of Moon-Children tend to be more gracile than those of controls as shown by our X-Ray studies. The Moon-Child skull tends to be brachycephalic. Observing many Moon-Children on the San Blas coast gave the impression that the malar eminences do not protrude as much as those of brownskins. X-Rays taken in the Walter position show a more narrow nasal region and the malar eminences actually farther in from the lateral periphery of the skull.

The forehead shape of Moon-Children is typical and differs from the normal. In profile there is a more gradual slope to the Moon-Child forehead. The teeth protrude less and the point of the jaw tends to be more sharp than in the controls.

The cartilage elements of Moon-Children are affected. How much of this may be due to the tropical sun we do not know. Not only is the nose of Moon-Children elongated due to cartilage hypertrophy, but the ears flare and cup due to cartilage overgrowth, while there develops a row of nodularities along the brim of the superior auricular cartilage. It is probable that in some Moon-Children the cartilages of the throat are somewhat hypertrophied because two out of six Moon-Children had a throat aperture

so small that the vocal cords could not be visualized with a speculum. One of these, and probably both, had trouble in swallowing. Chest shapes of Moon-Children tend to be abnormal.

Moon-Child Skin, Hair and Cancer

The head hair of albinos is invariably finer in diameter than that of controls. In childhood hair may be found at the sides of the face and always on the distal segments of the appendages.

Just as the eye color may darken with age so may the head hair, changing from white to yellow, and in some cases to red and even brown. This change is probably enhanced by the intense tropical sunshine.

The skin of the Moon-Child infant is pink, softened by short white hair all over the body. The skin appears extremely thin because capillaries are often evident.

As the child grows older he becomes exposed to sunshine, and huge freckles appear. Boys become blistered, and often carry a number of infected sunburn lesions simultaneously. Further exposure causes hypertrophy of the skin except under the freckles that will be sunken below the general hypertrophied surface. In this hypertrophied skin one notices seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas.

The skin of the girls is much more protected than that of the boys and accordingly, our statistics show that the Cuna Moon-Child boys die younger, on the average, than do the Moon-Child girls.

Thirty-Five Albino Indians were examined in Panama for presence of skin abnormalities and the severity of the abnormality was graded from 1-4+. Factors judged included the number of skin cancers, actinic keratoses, seborrheic keratoses, large freckles, small freckles, nonpigmented nevi and degree of skin infections. The number of plus marks for identical age groups in both sexes was averaged. These figures present a classical picture of the effects of exposure on skin. There was a gradual increase in severity of changes in both sexes with age. Although the average age of the males was less than that of the females, their skin changes were more severe as their overall exposure was greater.

The Cunas do not speak of a person after he has been buried, lest this interfere with the journey of his soul in the afterlife. For this reason it is difficult to learn about the cause of death. However, in recent years I was able to determine that among albinistic Moon-Children if they live to grow up, the chief cause of death is probably metastatic skin cancer.

It has been stated by Mac Fadden that the skin cancers of Moon-Children are squamous cell carcinomas. However, we find from biopsies that although squamous cells composed eight of ten skin cancers, the other two were basal cell carcinomas.

Of six Moon-Children brought to the Milledgeville State Hospital one had a Squamous cell carcinoma on the left cheek. The other two had squamous cell carcinomas on the right cheek and one on the right shoulder as well as a basal cell lesion on the left temple.

Moon-Child Teeth

Although the six Moon-Child boys and their pared brown controls all had gingival inflamation, calculus formation and other dental defects, there

were no striking differences between the two groups.

One Moon-Child had a malformed tooth. Two had malposition. One albino had super-numerary teeth. However, one control had malposition and one had poor tooth arrangement. Although actually the albinos had more defects, the number of individuals examined were so few that this difference cannot be considered of any importance, especially considering the fact that tooth anomalies are very common in the tribe.

Among the controls there were 35 decayed teeth; 36 among the albinos. The teeth do not reflect the weakness shown in the albino skeleton in general, and this is in conflict with reports of sporadic albino mammals found in nature.

Moon-Child Eyes

The fundi of the six Moon-Children were all typically albino with choroidal vessels seen clearly. Patches of the sclera were visable between the vessels and a more red area was observed where the normal macula should be located. In no case was a normal macular area noted. The optic disc was visualized in all cases, but appeared clearer in some due to the nature of the refractive area.

All the Moon-Children of San Blas show nystagmus which is of the ocular or fixation type with laterial movement of varying intensity. The Nystagmus does not appear until one month of age showing that it is a response to light rather than being due to a neurological defect.

All albino iridae are blue-gray in color with a light brown pigmented ring in the pupillary area and radiating



Cuna Indian girl with normal pigmentation.

brown-streaks in the ciliary area. Transillumination of the eye caused the iris to take on a typical glow. Slit lamp examination revealed a pale blue iris (with brown previously noted), which appeared thin and gave the illusion that one could almost see through it. Because of pigment in hair and eyes, many people deny that Moon-Children are true albinos.

All six albinos were severly myopic. This appears to be true for all Cuna albinos that I have examined during the past fourteen years. Thus, an elongated eyeball may be charactistic of the Moon-Child syndrome.

Corneal astigmatism was found in all six Moon-Children examined. Corneal curvature was normal except along the horizontal perimeter which was flattened in five albinos. A similar flattening was noted in the sixth, but in this case instead of being horizontal in both eyes the line of flattening was low laterally and high medially. From the standpoint of pigment gene



Infected mosquito bites in a Moon-Child boy. Resistance to infection is low in Moon-Children.



Cuna Indian Moon-Child girl. This girl died of skin cancer.

pleiotrophy these constant differences in shape of eyeball and lens curvature are of great importance.

Strabismus was found in all but one of the Moon-Children, and that in the one with the strongest physique. Three cases were of such long duration that the external lateral muscles cannot be made to function.

Vocal Tests of Moon-Children

Because I had found an analyzable change in voice to accompany various coat color mutations in rats and because Moon-Children voices to me to be soft and raised in pitch in adult males, we tested the six Moon-Child boys and their controls for quality of voice striking notes on the piano and having the boys imitate them. Speaking and singing were recorded on tape and again compared.

The tone quality of the Moon-Child voice, both vocal and speaking appears to be somewhat lighter and of a higher pitch than that of the brown.

The vocal range of the albinos was greater than that of the browns, but this may be due to the fact that the albinos tend to sing more.

It was observed that results obtained from the albinos were better than those of the browns. It might be assumed that music is an area that would give ego support to the albino in a field of accomplishment that might accord him some status and recognition within his culture since he is obviously different from the brown majority and physically weaker.

Laboratory Tests of Moon-Children

Three pairs of Indians, albino and control, had the following routine laboratory tests performed: complete blood count, sedimentation rate, sickle cell prep., thymol turbidity, cephalin flocculation, total cholesterol, potassium, sodium, uric H+, gloucose, urea nitrogen, protein bound iodine, urinalysis, and stool examination for ova and parasites. The others refused to cooperate in these tests, but such refusal will be obviated in the future.

Nothing noteworthy was discovered save that protein bound iodines were significantly higher in the albinos than in the browns. The albinos were in the range of thyrotoxicosis. This is

just the opposite of what would have been expected. However, these results are in line with the high basal metabolism figures for the black mutation in rats. Although these tests reveal nothing, it is known that Moon-Children, especially female, mature late.

Special laboratory tests made on all six albinos and their controls included haemoglobin, Hbg electrophoresis, serum electrophoresis, urinary acid secretion, Mosenthal's urinary concentration and blood typing for the presence of blood group antigens. A, B, O, D, E, C, c, e, Cu ^{s}, F, M, N, S, X, G, Le^{a}, Fe^{b}, Fa and Di^{a}. All Indians were O+. No significant differences were noted between albinos and browns with respect to other antigens. One of the brown controls was Diego positive, a fact of considerable importance to anthropologists.

Heart of the Moon-Children

Out of a sample of twelve Indians, to find, as we did, that five have slight or pronounced cardiac hypertrophies is indeed amazing. In the event that this incidence holds for other samples, the tribe should be studies for hereditary heart defects which it probably contains.

The QRS ventricular pattern of the S1 S2 S3 type is more frequent than the average (in 4 cases out of 5) among controls. It was observed but once among albinos.

In the albinos there is a tendency to left axis deviation; the tendency in normal controls is to right axis deviation.

In the albinos the tendency is for the horizontal position to predominate. In the controls the vertical electrical position predominates. There is no significant change in the rythm or in the 1-A and 1-1V conduction from both groups.

It will be interesting to note as further data are collected, whether these are merely chance associations or whether they represent pleiotropic tendencies of the albino gene and in contrast to the tendencies of its normal allel.

Intelligence of Moon-Children

The six Moon-Children and their brown controls were administered a battery of psychological tests: The Arthur Adaptation of the International Performance Scale (2 years 6 months to 12 years), the I.P.A.T. Culture Free Test of "G," three subtests of the Wechsler Adult Intelligence Scale, the Draw-A-Person Test, the Bender Gestalt Visual Motor Test, and the Rohrschach.

There are several limitations to the interpretation of the test data. First, there is a lack of norms for the Cuna Indians. Second, the Moon-Children have extremely poor vision. In addition, it was necessary to make most communication in Spanish through an interpreter. One of the examiners had Spanish as her mother tongue.

The materials collected were evaluated by five staff psychologists at the doctorate level. Where possible, statistical procedures were applied to the data.

The three formal intelligence tests, I.P.A.T. Culture Free Test, the Arthur Adoptation of the International Performance Scale, and three selected subtests from the Wechsler Adult Intelligence Test, gave high correlations, indicating that the tests were all approximating the same measure. The three subtests of the Wechsler Adult

Intelligence Scale were probably the best measure of intelligence of the two groups compared.

Only one intelligence test, the Arthur Adaptation of the International Performance Scale, showed a significant difference between albino and control (P=.004). This difference appears significant even on casual inspection. However, the value of the test may be questioned since it depends heavily on vision.

The remaining five tests showed no reliable differences between albino and control groups.

The conclusion of the I.Q. study is that no significant difference exists between the intelligence of Moon-Children and their controls. These conclusions are in keeping with my earlier interpretation but at variance with the generally accepted view.

A comparison of two of the albinos with two of the controls, both of whom were ranked as being high, in psychological health, reveals a basic difference in their level of emotional development and use of defense mechanisms. There is a striking masculine identification in the control group. They are more direct in expressing hostility, and openly aggressive and have an active interest in the opposite sex. On the other hand, the albinos reveal a passive, dependent feminine orientation. They show little active interest in the opposite sex, tending to relate to them on a pre-pubertal psychosexual level. They are more anxious, and typically use several defense mechanisms to ward off this anxiety. Some have a religious orientation while others rely more on intellectualization of their anxiety. Denial is pronounced. These defenses are weak, breaking down quickly under moderate stress, releasing the underlying hostility and aggression, or taking the form of withdrawal. Their reality is less accurate than that of the controls, being impaired by anxiety and leading to poorly conceived notions.

Psychiatric Examinations Of Moon-Children

Each albino and his paired control were given to a Spanish-speaking psychiatrist of M.D. training for psychiatric examination. (Spanish is the State language of San Blas.) He was instructed to look into nine areas of behavior; relations between parents; relations between mother and patient; relations between father and patient; relations between sibling and patient; also siblings and parents; sexual development and functioning; social development; relations to women; adaptational responses; and psychosomatic disorders.

From these examinations it would appear that the Moon-Children had a rather abnormal life, restrained in many activities by their physical condition. Four albinos (Three in their late twenties) have had no sex experience whereas two (in their middle thirties), the band master of Nargana and the dancing master of Ailigandi, have been able to attract girl friends by their public performance of music and dance. The dancing master started his sex experience at 31 years of age. That at least some of the albinos may be functional as males is shown by the fact that two of the albinos had sperm in their urine upon laboratory examination. Thus, masturbation probably provides a sexual adjustment among them.

One albino (the dancing master) remains at home and makes baskets, whereas another was for years the State-Treasurer of a local Indian store, so that a less rigorous life is sought by some of them. The town councils are considerate in manual labor demands upon the albinos.

The albinos of this group have had limited social experiences as compared with the controls. Some albinos had never left the San Blas Islands before their trip to Milledgeville and one has no formal education. However, they all appear as well adjusted as their brown counterparts with broader experience. Many albinos have strong family ties and have led productive, happy lives. By necessity (inability to stay in the sunshine) their work is generally in an intellectural sphere where over-compensation is usual. Religion serves as a major support for many of them who take a fatalistic view of life and blame their failures on their albinism which is "God's will." Sexual experience is as a rule, more limited than among the browns. This may reflect social taboos, social isolation or feelings of inadequacy. The one albino who boasted sexual relations with 22 women may well have been proving his adequacy to himself. Overcompensation, repression and massive denial are the major defense mechanisms in both groups. There is no difference between the groups in number of personality problems.

It is evident that much more data should be collected upon the psychiatric plight of the Moon-Children.

Discussion

The mutant albino rat (not the laboratory albino) is smaller in most respects than its normal gray controls, being 92.66% of normal in males and 98.33% of normal in females. Its thyroid is considerably reduced in both sexes. The hypophysis is slightly reduced in both sexes. The suprarenals are considerably reduced in males, slightly enlarged in females. The gonads in males are reduced to 91.00% those of females about a quarter of that amount. Olfactory bulbs are reduced to 92.69% in males and to 93.03% in females.

Such modifications of organs make slight changes in the behavior in rats. They are more tame than wild gray rats and their voices are raised in pitch from 400 cycles /sec. to 2800 cycles /sec. A raising of the pitch of voice was noted in the Moon-Child boys studied.

The reduction in size of olfactory bulbs in the mutant albino rat would be expected to dull the acuity of the sense of olfaction. Accordingly it was not surprising that we found evidences of such dulling in our garlic test.

Questioning of the Cunas brings the reply that Cuna Moon-Children are also dull in the sense of smell. A complete study should be made for accurate quantitative measurements of this deficiency.

While we are speaking about olfaction something about bodily odor should be inserted. Knowing that phenylketonurics and other human mutants with altered hair color have unique odors and knowing that at least one coat color in mice is accompanied by a special odor, I thought it worth while to ask about Moon-Children. Mothers of Cuna Moon-Children say that from birth the albinos have a

unique odor that is repulsive—smelling as though they needed a bath. This odor becomes worse when the albinos grow older, and even if they had just taken baths it was evident on the Moon-Child boys brought to Milledgeville. This is to be interpreted as evidence of an altered bio-chemical reaction associated with the albino syndrome.

In a study of wildness and tameness in rats Stone could distinguish the control from the mutant, but he could not find differences in intelligence. In a similar fashion one can note differences in temperament between the Moon-Children and brown skins, but no actual difference in intelligence was observed, contrary to common belief. However, the Moon-Children are psychiatrically disturbed by their handicap.

Summary of Moon-Child Study

The general impression of the somatotypes is that the brown skinned Cuna controls are more masculine, and that their muscles are better developed than those of the albinos. This impression is borne out in various ways. The average weight of the six Moon-Child boys studied at the Milledgeville State Hospital was almost 10% less than that of the browns. The bones of albinos are more gracile and bear less calcium deposit than those of the brown controls.

In chest circumference, head circumference, parietal diameter of the head, fronto-occipital diameter of the head, facial length, mandibular length, nasal length, interorbital length, interorbital distance, length of femur plus length of tibia, length of foot, wrist circumference, length of radius, length of humerus plus length of radius the browns are larger than the albinos, but the proportions in general remain relatively normal.

However, the length of the nose of the albino is proportionately greater than that of the controls. The Moon-Child tends to be brachycephalic and there is a more gradual slope to the Moon-Child forehead. The skull bones of the nasal region appear underdeveloped with less protrusion of the teeth. The point of the jaw tends to be more sharp in the albinos.

The albino ears flare more than do those of normals. The superior auricular cartilage hypertrophies, hardens and forms nodularities along the peripheral border of the pinna. The nasal cartilage elongates and possibly there is hypertrophy of the throat cartilages.

The hair of albinos is finer in diameter than that of the controls. In childhood hair may be found at the sides of the face and always on the distal segments of the appendages. The hair color may change with age from white through yellow to brown or even red brown.

The skin develops huge freckles and sunburn lesions. Continued exposure to tropical sunshine causes hypertrophy of the skin except under the freckles that will be sunken below the general hypertrophied surface. Degeneration takes place in the wrinkles of the skin of the inner surface of the elbow joint. In the hypertrophied skin of the body one notice seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas.

The eyes of Moon-Children are ordinarily blue-gray with some brown about the pupil, but may occasionally

change through various shades to brown. They are all myopic. Lateral nystagmus—slow to fast—develops in albinos at about one month of age. Strabismus is present in most albinos. The horizontal perimeter of the cornea is flattened in the six Moon-Children examined.

Laboratory tests showed nothing of importance but a physiological defect is suggested because of their high PBI, and distinctive body odor.

The voice of Moon-Children differs from that of the controls. It is weaker, has a higher pitch and less resonance.

The I.Q. of Moon-Child albinos that we studied is not in the mentally retarded range, but they do suffer psychiatrically.

The Moon-Children led an abnormal life, restrained in many activities by their physical condition. They are largely rejected by the opposite sex. The inability to compete physically often leads them to sedentary and intellectual pursuits. Because of their weaknesses and rejection they develop anxieties to which they react by over compensation or by regression.

Further data should be collected on the Moon-Children in all of the areas studied. An investigation of dreams and their interpretations that are so important to primitive peoples should reveal even more of their psychiatric condition. The possibility of early retarded physical development should be examined in the time of teething, walking and talking. Our examination of the Moon-Child syndrome reveals important alterations in morphology and behavior that appear as pleiotropic manifestations of the albino gene, much as one finds alterations of morphology, physiology and behavior associated with the presence of certain coat color genes in mammals.

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XLI

THE ALBINO MOON - CHILD RESEARCH PROJECT

Clyde E. Keeler, Sc. D., Principal Investigator
and
Irville H. MacKinnon, M.D., Co-Principal Investigator

This research project applies to man principles discovered by the principal investigator, during the past twenty years. It is supported by National Institutes of Health Grant GM no. 10472-01.

The principal investigator had found that black mutants occuring among Norway rats are tame by nature and that the cause of the behavior alteration was a gross modification of glands, sense organs and brain, these modifications all stemming developmentally from one recessive mutant gene pair.

We desired to learn if these principles also apply to the psychosomatic behavior of man because of their implications for psychology, psychiatry and medicine. The best variation for testing the principles appears to be albinism, but albinos occur only about once in ten thousand persons in the United States, in people of many different family origins that make them unfavorable for study. However, on the San Blas Coast of Panama near the Panama Canal lives a primitive tribe of 23,000 Indians called Cunas that have the highest incidence of albinism in the world. In 1962 we registered 144 Cuna albinos highly favorable for investigation because they have the same tribal hereditary and cultural background that make their reactions more uniform, just as inbred mice, cared for alike, give better results in pharmaceutical tests. The Cuna albinos are called Moon-children because their tribe believes that they were born white since the father or the mother looked too often at the moon during the pregnancy.

We were particularly interested in problems of Mental Retardation, as well as psychological and psychiatric evaluations involved in these studies. We were interested in any possible deviations in morphology and physiology, especially those that might contribute to deviations in behavior. We were interested in the skin cancers that are so often the cause of death among the albinos.

From May 15th to June 15th the principal investigator studied Moon-children on the San Blas Islands, accompanied by Dr. Donald Moyer, leading Dermatologist from the Gorgas Hospital. The principal investigator brought back to Milledgeville for two weeks of intensive laboratory study six albino boys and six

brown controls of similar ages. These were studied in the laboratories of the Milledgeville State Hospital by staff members and by two professors from the Medical College of Georgia. Finally, one albino was taken to the National Cancer Institute for two weeks and a half of further study and for removal of six cancerous lesions of the skin.

The principal investigators were assisted by Joseph Bohorfoush, M.D., Cardiologist, Haematologist; Serio Alverez-Mena, M.D., Cardiologist; Reichart Johnson, D.D.S., Dentist; George Courtney, Optometrist; Horace Stewart, Ph.D., Psychologist; Mrs. Virgina Balbona, M.A., Intern in Psychology; Helena Pessino, M.D., Radiologist; Mr. Walter Bowman, Technical Laboratory Director; Lillas James, M.D., Asst. Medical Geneticist; Julian Gomez, M.D., Psychiatrist; Hosea Balbona, M.D., Psychiatrist; Jose G. Mendosa, M.D., Psychiatrist; Joaquin Piedra, M.D., Psychiatrist; Carlos Maruri, M.D., Psychiatrist; Mr. Herbert Goldsmith, Music Therapist; Miss Becky Fuller, Laboratory Assistant; Miss Penny Edwards, Tissue Culturist; Virendra Mahesh, Ph.D., Biochemist; Hernan Dominguez, M.D., Tissue Culturist; and Jose Rauco, M.D., Otolaryngologist.

For those areas in which significant differences between Moon-children and brown controls were found, the findings will be outlined here by the specialists concerned.

ANTHROPOMETRICS OF MOON-CHILDREN

Lillas L. James, M.D.

Anthropometric measurements were made on the six Moon-child albinos and six controls for comparison.

Procedure:

Each Indian was carefully measured by the examiner for the determination of the following dimensions:

Weight. Patient was stripped of all clothing and weighed to the nearest one-eighth kilogram on Health-O-Meter Scale.

Height. Measured with patient standing flatfooted, chin up, on Health-O-Meter scales to the nearest one-eighth inch.

Chest Circumference Inhale. Measured by tape to nearest one-eighth inch at location of greatest circumference during forced inhalation.

Chest Circumference Exhale. Measured by tape to nearest one-eighth inch at location of greatest circumference during forced exhalation.

Wrist Circumference. Measured by tape to nearest one-eighth inch just proximal to ulnar head.

Length of Tibia. Measured by tape to nearest one-eighth inch as the distance from the proximal edge of the tibial tuberosity to the most prominent portion of the medial malleolus.

Length of Femur plus Length of Tibia. Measured to nearest one-eighth inch as the distance from the femoral head to the most prominent portion of the medial malleolus.

Metacarpal Dimensions. Measured by ruler to nearest millimeter on x-ray film taken at standard focal distance in RA views. The lengths were taken as the greatest vertical distances from distal to proximal points and the widths were taken as the smallest diameters of the shaft.

Head Circumference. Measured by tape to the nearest one-eighth inch from the glabella and the supraorbital ridges anteriorly to that part of the occiput postoriorly which gave the maximum circumference.

Parietal Diameter of Head. Measured by pelvimeter to nearest one-eighth inch as the greatest vertical distance between the two parietal bones.

Fronto-occipital Diameter of Head. Measured by pelvimeter to nearest one-eighth inch as the greatest vertical distance from the glabella to the occiput.

Facial Length. Measured to nearest one-eighth inch from the hairline to the inferior border of the mandibular symphysis.

Nasal Length. Measured by tape to the nearest one-eighth inch as the distance from the bridge of the nose to the nasolabial fold.

Manuometer deflections were then measured after maximal encouragement for high scores.

Results:

The figures were compiled and subjected to statistical analysis. It was readily noted that the mean dimensions, with the exception of nasal length, are all greater in the brown skinned controls than in the albinos. (All Indians were males between 20-40 years of age.) The difference in the means of some of these dimensions is significant. When expressed as a function of height the significance of the difference in means is less in all cases. This indicates a lesser overall body size for the albinos rather than altered body proportions. However, the greater mean length of the albino nose becomes statistically significant when it is expressed as a function of facial length, indicating that the albino nose is, in contrast, proportionately longer than the brown-skinned one, and the figures for the third metacarpal indicate that the albino shaft is proportionately narrower.

Manuometer deflections were analyzed with and without recordings for the one albino who was known to practice calisthenics. Without this pair the mean manuometer deflections for the browns was significantly greater than for the albinos. In summary, the statistics showed that the albinos were smaller, weaker, and had longer noses and narrower metacarpals than their brown counterparts.

Discussion:

Many factors are known to influence the overall size of the individual including genetic background, nutrition, physical exertion, chronic childhood diseases, endocrine abnormalities, etc. There is a possibility that several of these factors may be causally related to the smaller size of the albino children.

Keeler has shown that a gene affecting coat color in rats is pleiotropic in that it also effects body size and temperament. To date no such gene has been described for a human being. It is interesting to note that the average weight of the albinos was 90.4% of that of the controls, and the height of the albinos was 96.6% of that of the controls, near the 91.3% and 97.6% respectively that Keeler found for the albino mutant rat when he compared it with its parent strain. There is also mention in the literature of smaller size and weaker physique for albinos of other mammalian species. This smaller size of human albinos is consistent with the theory that a similar pleiotrophic gene may be represented by human albinism. The biochemical mechanism through which such an effect may be mediated has not been investigated in man or animal.

There is also a voluminous literature upon the adverse effects on growth of such varied chronic disease states as asthma, congenital heart disease, poliomyelitis, fibrocystic disease and chronic renal disease. Of late, much has been written in the Russian literature on the effect of exercise in childhood on the eventual size of the individual. Usually, of course, chronic disease and decreased exercise go hand in hand. As the albino child's outdoor activities are severely restricted because of his ocular and dermatological handicaps, his exercise rate is severely curtailed; and albinism must certainly be considered as much as a chronic disease state as a genetic syndrome effecting skin color. No comparative studies of nutrition have been made between the albinos and their brown skinned counterparts, but this too, may be a factor.

THE MOON-CHILD SKELETON

Helena Pessino, M.D.

Measurements so far strongly suggest that Moon-children tend to be shorter in height than normal controls of the same age. Their bones tend to be more gracile. This is quite noticeable in our x-rays of the bones of the wrist. The Moon-child hand and fingerbones are more slender and the solid periphery of these bones is narrower and less dense than in the normal hand. The carpal bones are small and delicately formed (See plates V and VII)

There are noticeable deviations from the normal in the Moon-child skull. The Moon-child skull tends to be brachycephalic. All six albinos examined were brachycephalic. This is not to say that brachycephaly does not occur in normals as one of the controls was brachycephalic.

After examining fifty or sixty Moon-children beyond puberty on the San Blas coast Dr. Keeler got the impression that their malar eminences do not protrude, on the average, as much as do those of the brown pigmented controls. Our x-rays of the skull taken in the Walter position revealed that this is probably a real difference, the six Moon-children studied having malar eminence lines at a greater distance from the lateral periphery of the skull. Closer inspection shows this to be due to a more narrow width of the nasal region. (See plate VII.)

There is a typical forehead shape that differs from the normal. In profile there is a more gradual slope to the Moon-child forehead, the teeth protrude less and the point of the jaw tends to be more sharp than in the controls.

Not only is the bony skeleton affected, but the cartilage elements may be altered as well. The narrow nose of the Moon-child is longer than that of the normal, presumably due to an increase in the cartilage which causes the nose to become hooked. The ears flare and cup and their cartilage becomes thickened and hard. A row of protuberances usually may be seen on the free edge of the pinna, due to nodularities forming on the superior auricular cartilage. Hypertrophy of cartilage may take place in the throat cartilages, as well, since two of the Moon-children examined by Dr. Jose Rauco had throat aperatures so small that the vocal cords could not be seen with a speculum and at least one and possibly both of these Moon-children have trouble swallowing solid food.

The chest of the albino in pair no.1 has the shape nearest to normal. He is a dancing master and practices his art regularly for long periods of time, blowing Pan's pipes vigorously throughout his dances.

MOON-CHILD SKIN, HAIR AND CANCER

Clyde Keeler, Sc. D.

The head hair of the albinos is invariably finer in diameter than that of the controls. In childhood hair may be found about the sides of the face and always on the distal segments of the appendages. (See plate V.)

Just as the eye color may darken with age so may the head hair, changing from white to yellow, and in some cases to red and even brown.

The skin of the Moon-child infant is pink, softened by short hair all over the body. It appears to be extremely thin and capillaries are often evident.

As the child grows older he becomes exposed to sunshine, and hugh freckles appear. Boys become blistered and often carry a number of infected sunburn lesions simultaneously. Further exposure causes hypertrophy of the skin except under the freckles that will be sunken below the general hypertrophied surface. In this hypertrophied skin one notices seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas. (See plate VI.)

The skin of the girls is much more protected than that of the boys and accordingly, our statistics show that the Cuna Moon-child boys die younger, on the average, than do the Cuna Moon-child girls.

Thirty-five albino Indians were examined in Panama* for the presence of skin abnormalities and the severity of the abnormality was graded from 1-4 +. Factors judged included the number of skin cancers, actinic keratoses, seborrheic keratoses, large freckles, small freckles, nonpigmented nevi and degree and severity of skin infections. The number of plus marks for identical age groups in both sexes was averaged. These figures present a classical picture of the effects of exposure on skin. There was a gradual increase in severity of changes in both sexes with age. Although the average age of the males was less than for the females, their skin changes were more severe as their overall exposure was greater.

The Cunas do not speak of a person after he has been buried lest this interfere with the journey of his soul in the Afterlife. For this reason it is difficult to learn about the cause of death. However, in recent years the principal investigator was able to determine that among the Albino Moon-children, if they live to grow up, the chief cause of death is probably metastatic skin cancer.

It has been stated by MacFadden that the skin cancers of Moon-children are squamous cell carcinomas. However, we find from biopsies that although squamous cell composed eight of ten skin cancers; the other two were basal cell carcinomas.

Of the six Moon-children brought to Milledgeville one had a squamous cell carcinoma on the left cheek. The other had two squamous cell carcinomas on the right cheek and one on the right shoulder as well as a basal cell lesion on the left temple.

* Donald Moyer, M.D., Dermatologist, Gorgas Hospital, accompanied the author and made these examinations.

THE MOON-CHILD EAR

by

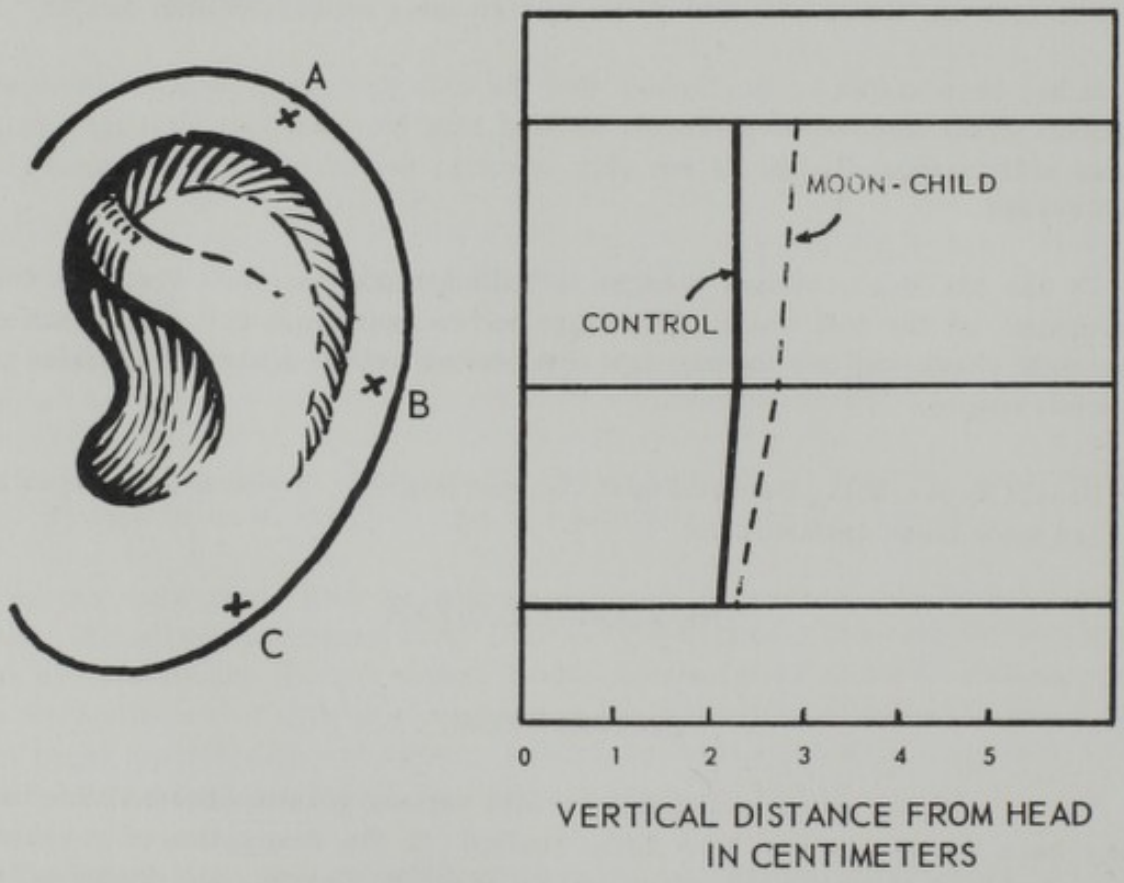
Beckwith Fuller

The association of ear modifications with various genetic abnormalities has long been known but has been little studied. In the description of psychical characteristics of mongoloid imbeciles, for example, the ears are described as small and badly formed. This refers to the cupped and flared ears that are so often present not only on mongoloids but also on individuals manifesting Marfan's syndrome. Heart and eye defects are associated in the above mentioned syndromes as well as in various other abnormalities whose associated ear variations have

not been documented. The possibility of such an ear modification associated with human albinism was therefor investigated in our survey of the total effects of the albino gene.

When the six albino Cuna Moon-child boys and their brown controls were first examined, what appeared to be a difference was noted in the ears of the two groups. The albinos seemed to be characterized by flared and cupped ears of hard texture with many nodularities arranged in a linear fashion along the brim, whereas, the controls seemed to be characterized by ears having less flare, normal texture, and no cartilage rugosities.These appeared to be differences that might be accociated with the albino gene.

In order to measure the amount of flaring of ears of albinos and controls, the border of the pinna was divided by three points (A, B and C) into four equal segments as shown in the diagram. At these points the perpendicular distance from the upper edge of the brim to the head was measured to determine the exact extent to which the ear protruded. These figures were tabulated for each albino and his brown control.



Text Figure 1. Distances of the brim of the ear from the head at the points A, B, C. Solid line connects points A, B, and C for normal controls. Dash line connects points A, B,C for Moon-children.

The results showed that the mean distance from the head to the border of the pinna in albinos was greater than the mean distance for controls at each of the points A, B, and C. The measurements also showed that the extent of flare was greatest at the top of the ear with a marked inclination toward the head at B and C, in that order. See figure 1. The difference between the albino mean and the control mean at point A was significant. ($.05 > P > .02$). For points B and C the differences are not statistically significant. However, when the distances for each individual were divided by his height, to take account of the difference in body size between albinos and their larger controls, the disparity between the albino means and the control means became even greater and more significant. It was statistically significant for point A ($.01 > P \geq 001$) and also for B ($.1 > P > .05$).

Inspection showed that each albino's ears were very hard and hypertrophied whereas the ears of the controls were in every case of normal thickness and pliability. The brims of one or both ears of the albinos also exhibited cartilage nodularities not found on the controls. One explanation for the hard texture of the ears could be degenerative changes in the skin due to exposure to the sun.

Other observations on the albinos in this project confirmed that their unpigmented skin is highly sensitive to sunlight, and for those who worked outdoors severe lesions and skin cancers were quite common. Moreover, all the exposed skin was thick, tough and dry.

The presence of nodularities of hypertrophied cartilage along the brim of the ear suggested that the hardness was undoubtedly due to an unusual overgrowth of cartilage. This condition reminds one of the cartilage hypertrophy that takes place in grey lethal rats, an inherited syndrome in which developing cartilage differentiates abnormally. This abnormal development in the rat produces a chain of symptoms that eventually cause death. Elastic cartilage, such as is present in the ear, is also found in the larynx, and preliminary studies show that at least two of the Moon-child albinos have difficulty in swallowing, perhaps indicating an abnormal cartilage development here. This could lead to serious consequences. Whether this abnormal development is triggered by the sun or develops independently we do not know at present.

The findings of this study on the Moon-child albino ear indicate that there is indeed an ear defect associated with the albino gene when it develops in the tropics, just as there are ear manifestations associated with other genetic abnormalities. The tropical sunshine is suspected as a triggering factor in producing flare, hypertrophy of skin and cartilage that forms brim nodularities of the Moon-child albino ear.

MOON - CHILD TEETH

Reichart Johnson, D.D.S.

All twelve Indians had gingival inflammation, calculus formation and other dental defects, common in persons with no professional attention. In comparing the controls and test groups there were no striking differences between the two groups.

One Moon-child albino had a mal-formed tooth. Two albinos had mal-position. One albino had supernumerary teeth. However, one control had mal-position and one had poor tooth arrangement. Although the albinos had more defects, the number of individuals examined was so few that this difference cannot be considered of any importance, especially in view of the fact that tooth anomalies are frequent in this tribe.

Among the controls there were 35 decayed teeth; 36 among the albinos.

The teeth do not reflect the weakness of development shown in the albino skeleton in general.

MOON - CHILD EYES

George Courtney, O. D.

The fundi of the six Moon-children were all typically albino with choroidal vessels seen clearly. Patches of the sclera were visible between the vessels and a more red area was observed where the normal macula should be located. In no case was a normal macular area noted. The optic disc was visualized in all cases, but appeared clearer in some due to the nature of the refractive error.

All the Moon-children of San Blas show nystagmus which is of the ocular or fixation type with lateral movement of varying intensity. The nystagmus does not appear until one month of age showing that it is a response to light rather than being due to a neurological defect.

All albino iridae are blue-grey in color with a light brown pigmented ring in the pupillary area and radiating brown streaks in the ciliary area. Transillumination of the eye caused the iris to take on a typical pink glow. Slit lamp examination revealed a pale blue iris (with brown previously noted), which appeared thin and gave the illusion that one could almost see through it.

All six Albinos were severely myopic. This appears to be true for all Moon-child Albinos observed by Dr. Keeler in San Blas during the past fourteen years. Thus, an elongated eyeball may be a characteristic manifestation of the albino gene. This finding is of great importance to the subject of pleiotropy, and curvature of the cornea will be measured in the laboratory in the future.

Strabismus was found in all but one albino who was of the strongest physique among the Moon-children. Three cases were so extreme and of such long duration that the external lateral muscles cannot be made to function.

VOCAL TESTS OF MOON-CHILDREN

Herbert Goldsmith, R.M.T.

The six Cuna albinos and their paired brown controls were tested for Quality, Intonation and Range by striking notes on a piano and having the subject try to produce the same pitch.

As a result of this effort we may say:

(1) The tone quality of the Albino voice, both vocal and speaking appears to be somewhat lighter than that of the Brown Indian.

(2) Of the subjects tested it appears that the vocal range of the Albino, in general, is higher than that of the Brown.

(3) It was observed that results obtained from the Albinos were better than those from the Browns. It might be assumed that music is an area that would give ego support to the Albino in a field of accomplishment that might accord him some status and recognition within his culture since he is obviously different from the Brown majority and weaker physically.

If one grades each albino and control with plus marks in columns of good, medium or poor for the three items of Quality, Intonation and Range the Albinos have 10 plusmarks in the "good class" as against 6 plusmarks for the Controls. The Albinos have 4 plusmarks in the "medium class" as against 4 plusmarks for the Controls. The Albinos have 4 plusmarks in the "poor class" against 4 plusmarks for the Controls. Thus, the Moon-child Albinos are thought to have slightly better voices in general on these three criteria taken together, but where quality of voice alone is considered 2 of the Albinos had "good quality" compared with 4 with "good quality" among the Brown controls.

LABORATORY TESTS OF THE MOON-CHILDREN

Walter Bowman, Sc. M.

Three pairs of Indians, albino and control had the following routine laboratory tests performed;complete blood count, sedimentation rate, sickle cell prep, thymol turbidity, cephalin flocculation, total cholesterol, potassium, sodium, uric H+, glucose, urea nitrogen, protein bound iodine, urinalysis, and stool examination for ova and parasites. The others refused to cooperate in these tests, but such refusal will be obviated in future studies.

Several of the Indians had high sedimentation rates; of these, one had a relative lymphocytosis. These values probably reflect a mild viral infection which affected most of the Indians during some period their stay.

The high eosinophil counts reflect the high percentage (controls 2 - albinos 2) of Indians found to have round worm ova on stool examination.

All Indians tested were found to have high thymol turbidities and /or high cephalin flocculations. However, none of the Indians was found to bear clinical evidence of liver disease. The abnormal values probably reflect low grade chronic parasitic infections.

The average uric acid value for the combined group was 5.4mg%, considerably above the normal range of 1 - 3mg%. No significant differences between the two groups were noted. We know of no increase in the incidence of gout among these people. At present these high values are unexplained.

The protein bound iodines were significantly different in the two groups. Two of the three albinos were actually in the range of thyrotoxicoses, while two of the browns were in the range of hypothyroidism. Both of the groups are known to have high iodine diets (fish), so this does not explain the difference. Further thyroid studies are necessary to account for this quite unexpected result.

All other examinations were within the normal range with no significant difference noted between the two groups.

SPECIAL LABORATORY TESTS ON THE MOON - CHILDREN

Lillas James, M. D.

Special laboratory tests include Hemoglobin, Hbg electrophoresis, serum electrophoresis, urinary acid excretion, Mosenthal's urinary concentration and blood typing for the presence of A,B,O,D,E,C,c,e,Cu^8,F,M,N,S,K,G,Le^a,Le^b,Fy^a, and Di^a, antigens. All Indians were O+. No significant difference were noted between albinos and the browns with respect to the other antigens. One of the brown controls was Diego postive, a fact of considerable importance to anthropologists.

Ridge counts of the fingerprints calculated according to the method of Bonnevie were prepared. Nothing of significance was found.

HEART OF THE MOON - CHILDREN

Sergio Alverez - Mena, M.D. and Joseph Bohorfoush, M.D.

Albino, Pair #1, is a borderline case of left ventricular hypertrophy. Albino, Pair #4, is a definite case of left ventricular hypertrophy. X-ray showed moderate splenomegaly. Albino, Pair #6, has a slight left ventricular hypertrophy, revealed by x-ray. Brown skin Pair #6, is an unequivocal case of right ventricu- hypertrophy. Brown skin, Pair #5, has a definite left ventricular hypertrophy.

Out of a sample of twelve Indians, to find five having slight or pronounced cardiac hypertrophies is indeed amazing. Further research must determine whether or not this high incidence holds for other samples. In the event that it does hold, the tribe should be studied for hereditary heart defects which it probably contains.

The QRS ventricular pattern of the S1 S2 S3 type is more frequent than the average (in 4 cases out of 5), among the controls, but observed but once among the six albinos.

In the albinos there is a tendency to left axis deviation;the tendency in the normal controls is to right axis deviation.

In the albinos the tendency is for the horizontal position to predominate. In the controls the vertical electrical position predominates. There is no significant change in the rhythm or in the I-A and I-IV conduction from both groups.

INTELLIGENCE OF MOON-CHILDREN

Horace Stewart, Ph.D.
Assisted by Virginia Balbona and Sue Reynolds

The six Moon-children and their six Brown controls were administered a battery of psychological tests: The Arthur Adaptation of the International Performance Scale (2 years 6 months to 12 years), the I.P.A.T. Culture Free Test of "G", three subtests of the Wechsler Adult Intelligence Scale, the Draw-a-Person Test, the Bender Gestalt Visual Motor Test, and the Rohrschach.

There are several limitations to the interpretation of the test data. First, there is a lack of norms for the Cuna Indians. Second, the Moon-children have extremely poor vision. In addition, it was necessary to make all communication in Spanish through an interpreter. This latter difficulty can be eliminated by using a Cuna interpreter.

The materials collected were evaluated by five staff psychologists at the doctoral level. Where possible, statistical procedures were applied to the data.

The three formal intelligence tests, I.P.A.T. Culture Free Test, the Arthur Adaptation of the International Performance Scale, and three selected subtests from the Wechsler Adult Intelligence Test, gave high intercorrelations, indicating that the tests were all approximating the same measure. The three subtests of the Wechsler Adult Intelligence Scale were probably the best measure of intelligence of the two groups compared.

There was only one intelligence test, the Arthur Adaptation of the International Performance Scale, that showed a significant difference between albino and control ($P = .004$). This difference appears significant even on casual inspection. However, the value of this test may be questioned since it depends heavily on vision.

The remaining five tests showed no reliable differences between albino and control groups.

The conclusion of the I.Q. study is that no significant difference exists between the intelligence of Moon-children and their controls. These conclusions are in keeping with the earlier interpretations of the principal investigator.

A comparison of two of the albinos with two of the controls, both of whom were ranked as being high in psychological health, reveals a basic difference in their level of emotional development and use of defense mechanisms. There is a striking masculine identification in the control group. They are more direct in expressing their hostility, are openly aggressive, and have an active interest in the opposite sex. On the other hand, the albinos reveal a passive, dependent, feminine orientation. They show little active interest in the opposite sex, tending to relate to them on a pre-pubertal psychosexual level. They are more anxious, and typically use several defense mechanisms to ward off this anxiety. Some have a religious orientation while others rely more on intellectualization of their anxiety. Denial is pronounced. These defenses are weak, breaking down quickly under moderate stress, releasing the underlying hostility and aggression, or taking the form of withdrawal. Their reality is less accurate than that of the controls, becoming impaired by anxiety and leading to poorly conceived notions.

PSYCHIATRIC EXAMINATIONS OF MOON-CHILDREN

Julian Gomez, M.D.

Assisted by Hosea Balbona, M.D. Adolph Ponce de Leon, M.D.

Jose Mendosa, M. D., Joaquin Piedra, M. D., Carlos Maruri, M.D.

Each albino and his paired control were given to a Spanish-speaking psychiatrist of M.D. training for psychiatric examination. (Spanish is the State langauge in San Blas). He was instructed to look into nine areas of behavior: relations between parents; relations between mother and patient; relations between father and patient; relations between siblings and patient, also siblings and parents; sexual development and functioning; social development; relations to women; adaptational responses; and psychosomatic disorders.

From these examinations it would appear that the Moon-children lead a rather abnormal life, restrained in many activities by their physical condition. Four albinos (three in their late twenties) have had no sex experience whereas two (in their middle thirties), the band master of Nargana and the dancing master of Ailigandi have been able to attract girl friends by their public performances of music and dance. The dancing master started his sex experience at 31 years of age. That at least some of the albinos may be functional as males is shown by the fact that two albinos had sperm in their urine upon laboratory examination. Thus, masturbation probably provides a sexual adjustment among them.

One albino (the dancing master) remains at home and makes baskets, whereas another was for years the secretary-treasurer of a local Indian store, so that a less rigorous life is sought by some of them. The town councils are considerate in manual labor demands upon the albinos.

The albinos of this group have had limited social experiences as compared with the controls. Some albinos have never left the San Blas Islands and have had no formal education. However, they appear to be as well adjusted as their brown counter-parts with broader experience. Many have strong family ties and have led productive, happy lives. By necessity, (inability to stay in the sunshine) their work is generally in an intellectual sphere where over-compensation is usual. Religion serves as a major support for many of them who take a fatalistic view of life and blame their failures on their albinism which is God's will. Sexual experience is as a rule more limited than in the browns. This may reflect social taboos, social isolation or feelings of inadequacy. The one albino who boasted sexual relations with 22 women may well be proving his adequacy to himself. Overcompensation, repression and massive denial are the major defense mechanisms in both groups. There is no difference between the groups in number of personality problems.

It is evident that much more data should be collected upon the psychiatric plight of the Moon-children.

SUMMARY OF MOON-CHILD STUDY

Clyde E. Keeler, Sc.D., and Irville H. MacKinnon, M.D.

The general impression of the somatotypes is that the brown skinned controls are much more masculine, and that their muscles are better developed than those of the albinos. This impression is borne out in various ways. The average weight of the six Moon-child boys was almost 10% less than that of the browns. The average height of Moon-child boys was 3% less than that of browns. The bones of albinos are more gracile and bear less calcium deposit than those of the brown controls.

In chest circumference, head circumference, parietal diameter of the head, fronto-occipital diameter of the head, facial length, mandibular length, nasal length, interorbital distance, length of femur plus length of tibia, length of tibia, length of foot, wrist circumference, length of radius, length of humerous plus length of radius the browns are larger than the albinos, but the proportions in general remain relatively normal.

However, length of nose of the albinos is proportionately greater than that of the controls. The skull bones of the nasal region appear to be underdeveloped, causing a slight change in shape of face.

The albino ears flare more than do those of normals. The superior auricular cartilage hypertrophies, hardens and forms nodularities along the peripheral border, of the pinna. The nasal cartilage elongates and possibly there is hypertrophy of the throat cartilages.

The hair of albinos is finer in diameter than that of the controls. In childhood hair may be found about the sides of the face and always on the distal segments of the appendages.

The skin develops hugh freckles and sunburn lesions. Continued exposure to sunshine causes hypertrophy of the skin except under the freckles that will be sunken below the general hypertrophied surface. Degeneration takes place in the wrinkles of the skin of the inner surface of the elbow joint. In the hypertrophied skin of the body one notices seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas.

The eyes of Moon-child albinos are myopic. Lateral nystagmus, -slow to fast - develops in albinos at about one month of age. Strabismus is present in most albinos.

The voice of albinos differs from that of controls. The albino voice is weaker and has less resonance.

The I.Q. of Moon-child albinos is not in the Mentally Retarded range, but they suffer psychiatrically.

The Moon-children lead an abnormal life, restrained in many activities by their physical condition. They are largely rejected by the opposite sex. The inability to compete physically, often leads them into sedentary and intellectual pursuits. Because of their weakness and rejection they develop anxieties to which they react by overcompensation or by regression.

Further data should be collected on the Moon-children in all of the areas studied. An investigation of dreams and their interpretation that are so important to primitive peoples should reveal even more of their psychiatric condition. The possibility of early retarded development should be examined, in the time of teething, walking and talking.

PLATES

I-IV The six Cuna Moon-child albino boys and their brown controls studied intensively at the Milledgeville State Hospital.

V Left: Hypertrophy of the auricular cartilage of two Moon-child boys with development of nodularities along the border of the pinna.

Center: A hand of two Moon-child boys showing weakness of development.

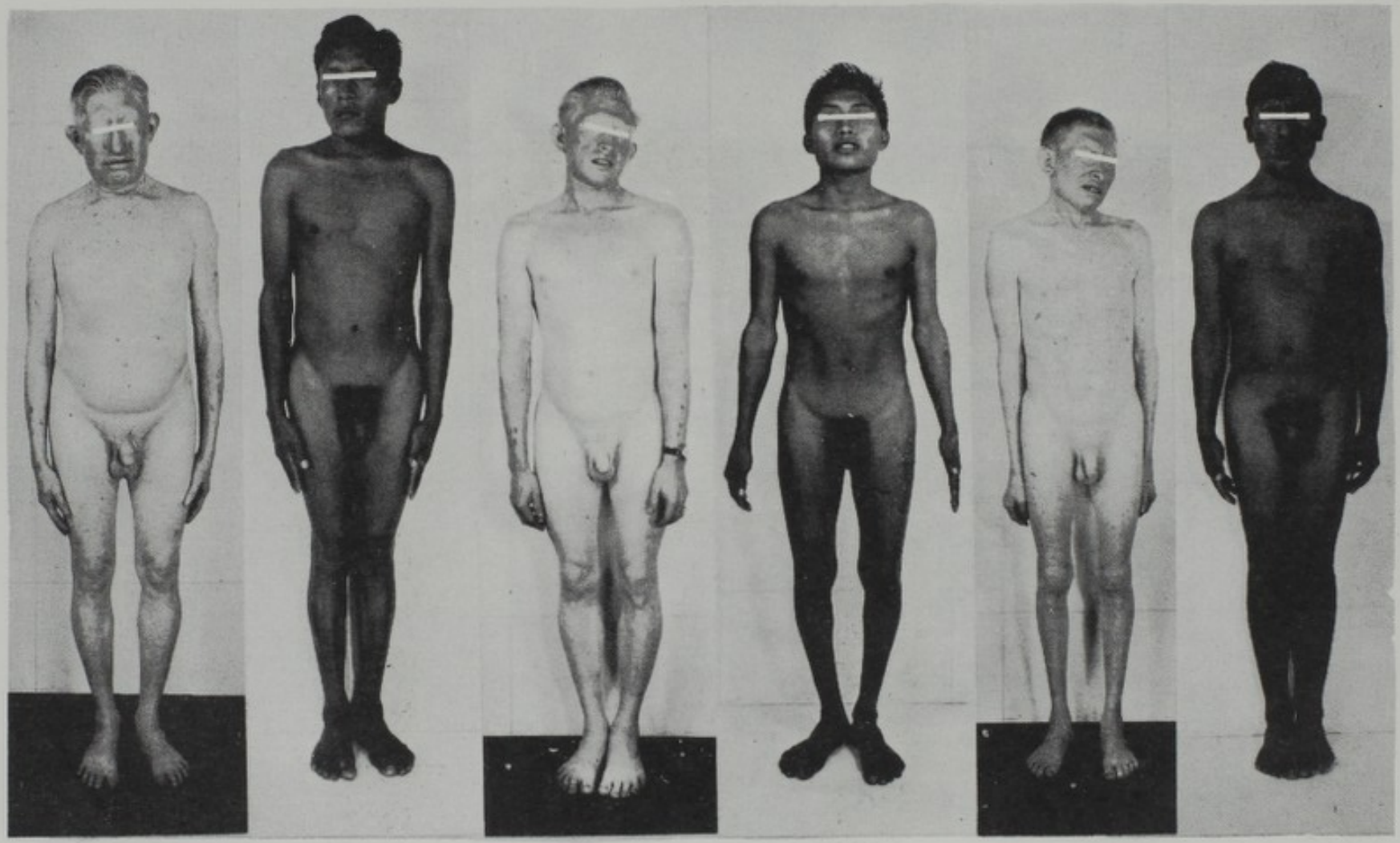
Right: Arm and hand of a Moon-child boy showing hair growth. The brown controls are devoid of arm hair.

VI Left and Center: Lesions on the skin of Moon-child 3a.

Right: Hypertrophy of the skin of the arm of Moon-child 3a as well as degenerate furrows where the skin wrinkles during flexion.

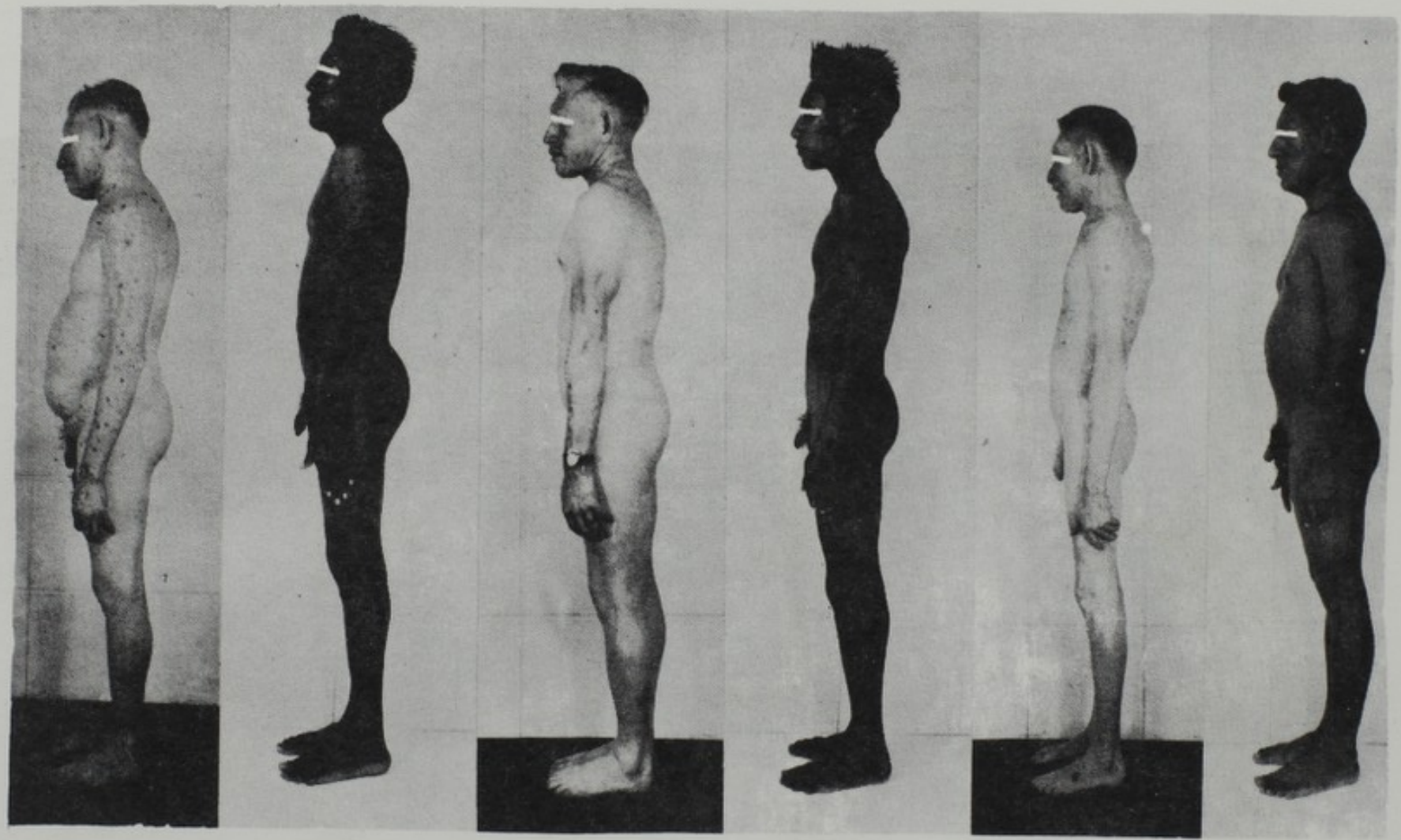
VII X-rays, above: Skull of a brown control boy and a Moon-child, followed by the face profile of a brown control boy and a Moon-child.

below: Walter position skull of a brown control boy and a Moon-child followed by the hand of a brown control boy and a Moon-child.



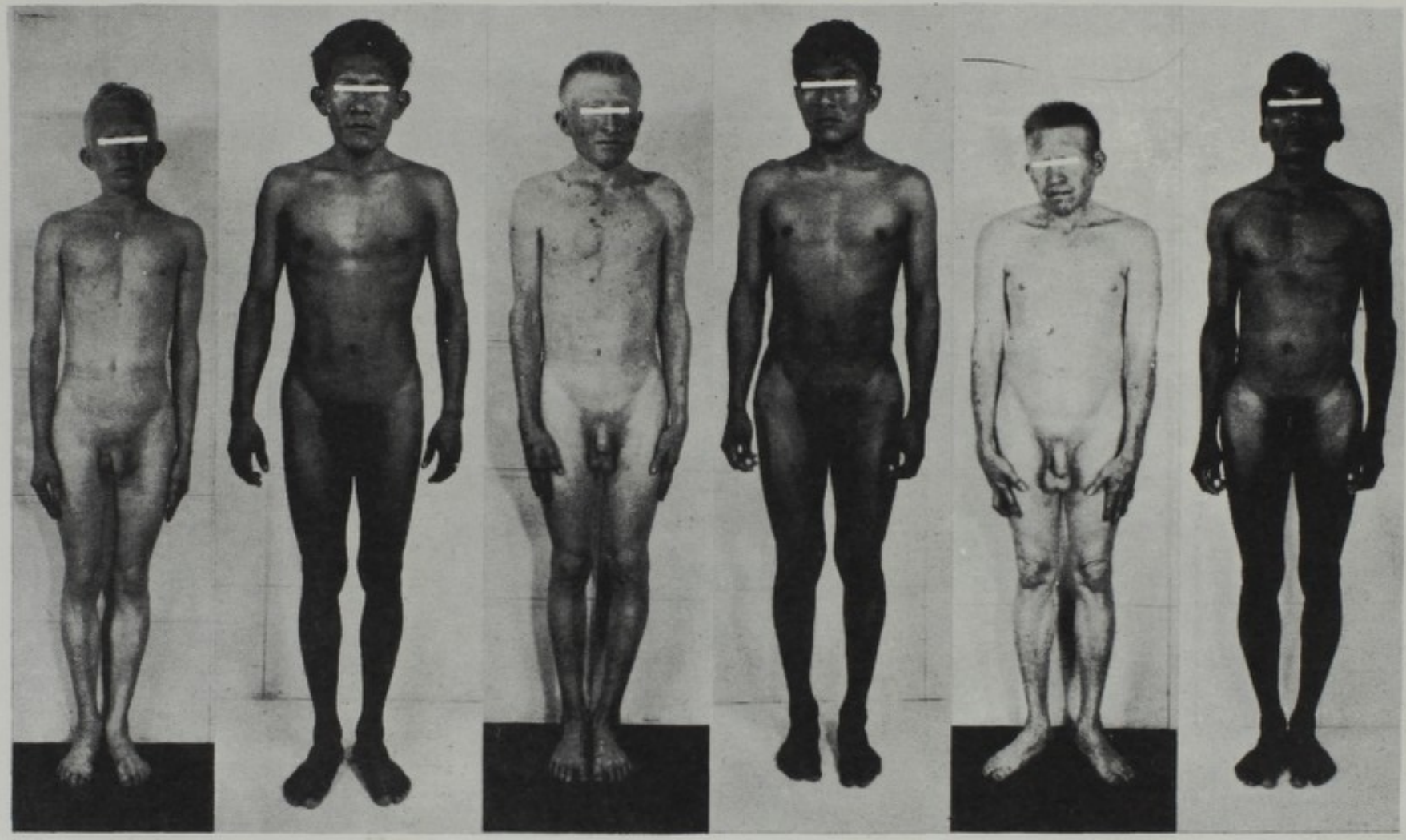
1a 1b 2a 2b 3a 3b

PLATE I



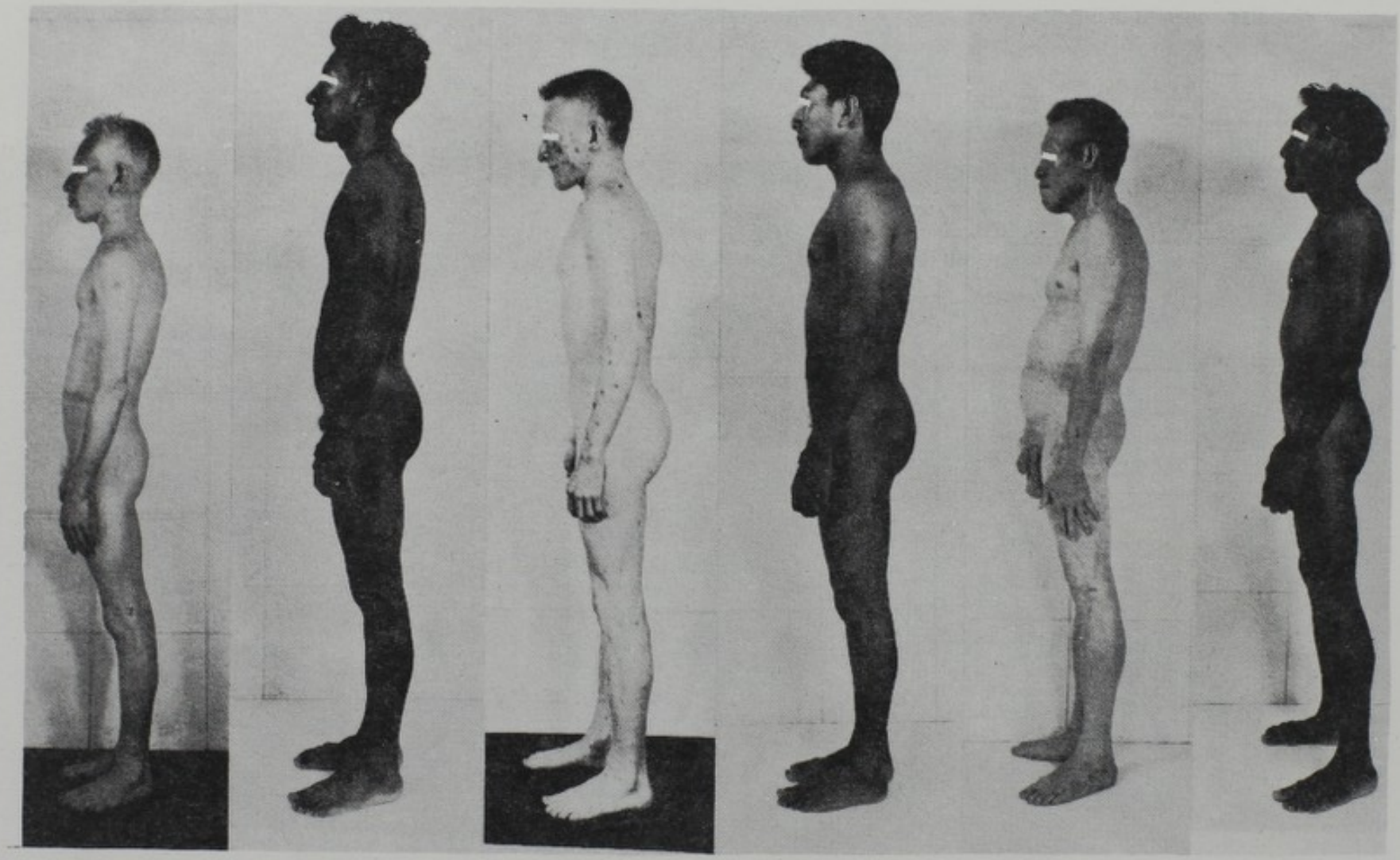
1a 1b 2a 2b 3a 3b

PLATE II



4a 4b 5a 5b 6a 6b

PLATE III



4a 4b 5a 5b 6a 6b

PLATE IV

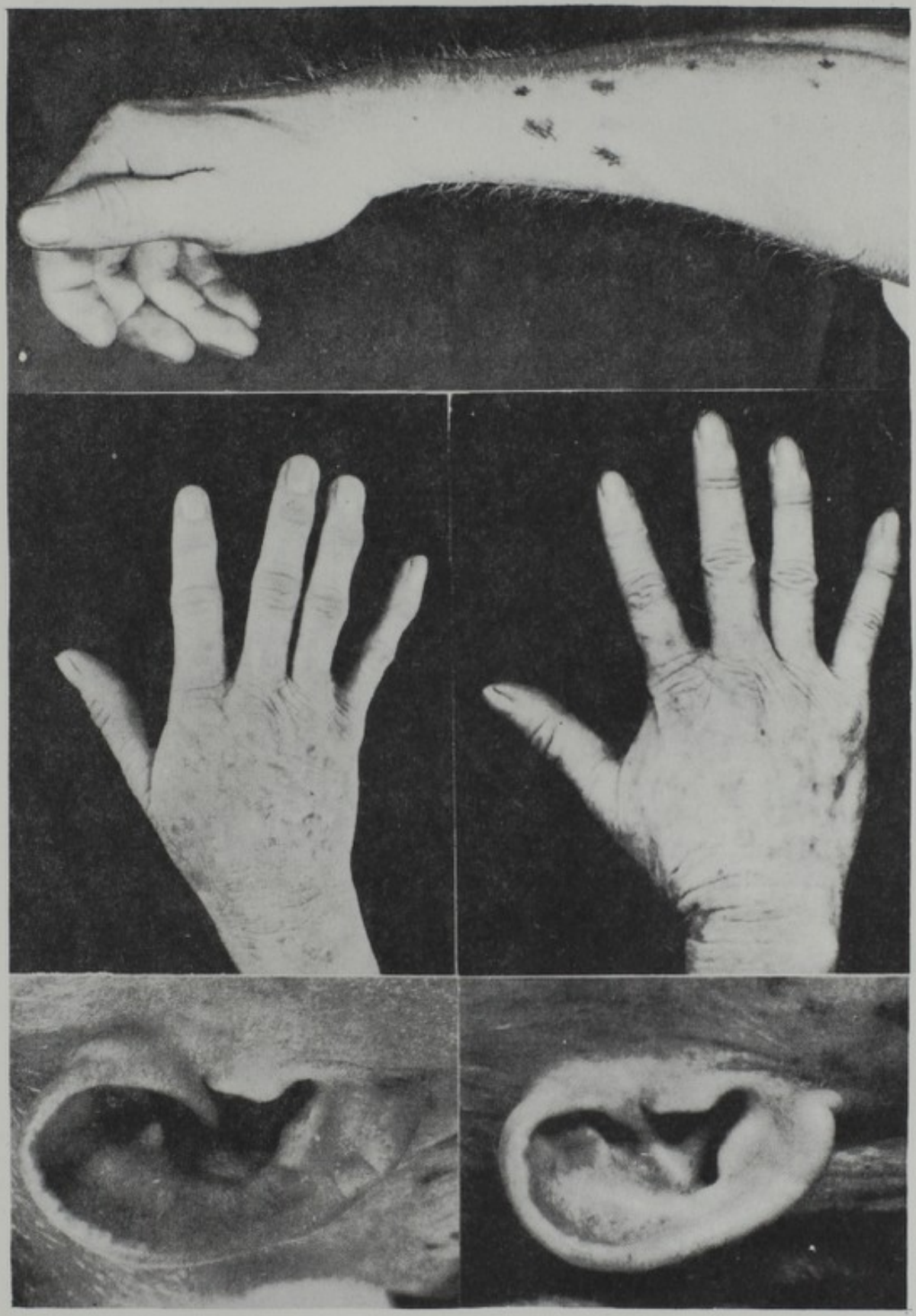


PLATE V



PLATE VI

PLATE VII

XLII

"ALBINISM" — VISUAL DEFECTS OF THE CARIBE CUNA MOON-CHILD*

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THE MOON-CHILDREN

The Cuna Indians of San Blas province of lower Panama are noted for their large golden nose rings, colorful appliqued cotton blouses and for the fact that they possess the highest incidence of albinism in the world. This is in the neighborhood of forty-five in ten thousand. Various sources quote the normal incidence of albinism in Europeans as one in ten thousand. These Cuna Indians live in a rather primitive culture, characterized by strange animistic customs and devil appeasement ceremonies. There are various stories that account for the origin of the Moon-children. Some Indians invoke parental impressions to explain their occurrence, because the Cuna believe that all sorts of markings may be due to the mother-to-be or her husband having looked at the wrong things. When Moon-children are produced, one or both parents may have gazed too long at the moon, cotton or other white objects.[1] Albinos are said to be less sinful than other persons and therefore on better terms with Tiolete, the Sun-god. Because of this better behavior on earth, Moon-children will receive better houses in heaven. Others will not be permitted even to look into these heavenly mansions unless they have made friends with eight Moon-children on earth. At the time of eclipse only the albinos are holy enough to rush out with bows and arrows to shoot and kill the earth-mother's Sky Dragon or placental monster, who is trying to end the world by swallowing up the sun and moon.[2]

For the past fourteen years these people have been under study by one of us, C.E.K., who is Medical Geneticist at Milledgeville State Hospital. C.E.K. has made ten visits to these islands. The current study involved the visit of twelve Indians to Milledgeville State Hospital for a battery of physical, psychological and psychiatric examinations.**

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Amer. J. Uptometry 41: 283- 292. 1964.

The Cuna population has been estimated at from four hundred thousand to seven hundred thousand at the time of Columbus. Due to frequent conflicts with the Spaniards with their slave trade, and a campaign of extermination understaken by the conquistadores, their number today is somewhere around twenty-three thousand. Approximately one hundred and forty-four are albinos. During the past 450 years the Cuna have successfully warded off civilization. They still live in a closely knit, inbred society with little inter-marriage between inhabitants of the various villages. They have a great fear of foreigners. Occasional alliances in the past have often resulted in massacre of the intruders or the hybrid children. Formerly, the Cunas practiced infanticide to eliminate most of the Moon-child homozygotes. This is probably still carried on to some extent in the more remote villages. Infanticide may have been a eugenic measure or an expression of pity, knowing the albinos would fare poorly in the struggle for survival. For the same reasons, marriage of the Moon-children was taboo. This taboo was enforced by the town council which still has strict control over many Cuna activities.

With the encroachment of civilization the practice of infanticide and taboos on marriage are disappearing. The strict control of the town council is breaking down. There is increased emphasis on the rights of the individual which may result in an even higher incidence of albinism in the future. The great reduction in numbers of the total population of the tribe, a social preference for light colored heterozygotes, as well as the town inbreeding pattern, has spread the Moon-child gene to a greater percentage of inter-marrying families making random matings more frequent between heterozygotes. These more frequent heterozygous marriages have increased the incidence of Moon-child births.[3]

ALBINISM

The albino, with his characteristic lack of coloring, and characteristic "red eyes," shows a wide range of ocular anomalies; photophobia is constant, a low degree of myopia is frequent, as is convergent squint. Visual acuity is poor owing to lack of differentiation of the macula and the consequent nystagmus.[4]

The errors of refraction are usually severe with astigmatism being an important component. In a random sampling of mixed albinos there may be both hypermetropes and myopes, but seldom is emmetropia present. Clinically five types of albinism are recognized.

(1) Complete generalized albinism: There is a total lack of pigment throughout the body, hair and eyes. Strabismus and nystagmus are usually severe. Visual acuity is very poor and the iris transmits light.

(2) Incomplete generalized albinism: There is some pigment in the hair, eyes and skin. The iris, although showing some coloration, transmits light. Visual acuity is impaired and nystagmus and strabismus are severe. Among the Cunas is a boy containing one gene for Moon-child and one for European blond credited to the shipwreck of an English sailor. This individual seems to fall in this class.

(3) Albinoidism: In this type the hair and skin are only slightly darker than albinos but visual symptoms are absent and the iris does not transmit light. This condition may be present only in early life.

(4) Ocular: This type is characterized by an incomplete absence of pigment in the eyes only, with accompanying symptoms. Ocular albinism may correspond to pink eyed pigmented types found in many mammals.

(5) Albinotic Fundus: This type is defined as a lack of pigment in the fundus only. In this variety the macula may or may not be developed, leading to the possibility of two distinct sub-types.

Nystagmus is always present in complete albinism. It is also frequently present in partial albinism. Since the pigmentation also often increases later on, nystagmus may be seen in patients without conspicuous albinism, but the patient's history may reveal he was very "blond" early in life and the ophthalmoscope may show a sub-albinotic appearance in the anterior part of the fundus.[5] This is in keeping with the five classifications given. The nystagmus is of the fixation or ocular type. The nystagmus occurs in every possible direction, with the extremes of amplitude and frequency. It is seldom directed; that is, it is made up generally of two components which are of about the same rapidity. It occurs in persons who were born with very poor vision due to any cause whatever, but it seldom occurs in persons who are blinded later in life. Since it usually lacks a quick and slow component, both movements having an equal time value, frequently it is termed a nystagmoid movement, rather than true nystagmus.[6]

Albinism is an hereditary anomoly caused by a bio-chemical error in the metabolism of melanin. In this condition the mutant gene results in a deficiency of the enzyme tyrosinase in the melanocytes of the skin. The melanocytes, however, are present in normal numbers. The deficiency in tyrosinase interferes with the conversion of tyrosine to dopa, which is ultimately converted to melanin. Since melanin cannot be produced in adequate amounts, albinos have a non-pigmented white skin, white hair and non-pigmented iris.[7]

In complete or incomplete total albinism, the inheritance is reces-

sive in character. In albinoidism it is strictly dominant. Albinism affecting the eyes only is inherited as a sex linked recessive.

It is not known whether Moon-child albinism is identical with albinism in the caucasian race. This could not be determined unless a cross were made between the two types. Moon-child albinism differs in some details from caucasian albinism. This may be due to the greater amount of pigment normally present in Indians or to climatic conditions.

MOON-CHILD ALBINISM

Severe eye defects and unpigmented skin with atropic changes are characteristic of all of the albinos. In general the albinos are smaller, lass masculine and with less muscle development than the brown skin controls. None of the Cuna Moon-children appear to be mentally retarded as is sometimes found in caucasian albinos. This may be due to the fact that among caucasians where albinism is rare, it often appears due to cousin marriage. This is likely to bring to the surface at the same time recessive mental defects of many sorts. Among the Cunas where albinism is so very frequent, most is not due to cousin marriage and hence the recessive mental defects are not noticeably associated with it.

The skin of the Moon-children is infant pink and appears to be very thin with capillaries often evident. Skin cancer is fairly frequent, probably caused by exposure to the tropical sun. Short white hair can be observed all over the body. The head hair is very fine and of a light yellow color. In contrast to the smooth skinned controls, Cuna Moon-children usually have hair on the distal segments of the appendages. It is white and sometimes as much as an inch long.

Intelligence tests reveal no significant difference between the Moon-children and their controls. In the psychiatric evaluation, the albinos were found to have had limited social experiences when compared to the controls. However, they appeared to be as well adjusted as their brown counterparts. Over compensation, repression and massive denial are the major defense mechanisms in both groups. There is no difference between the groups in the number of severe personality problems.

OCULAR FINDINGS

Comparisons of the various pairs are shown in Tables 1, 2 and 3. A casual examination will reveal an abnormally high incidence of pathology due to trauma in the control group. This reflects the lack of medical facilities in the area and the more restricted activities of the Moon-children. Early adolescence brings an almost complete withdrawal from athletic activities on the part of the albino group. The

TABLE 1

	External Examination		Pupil Reflexes		Iris	
	Control	Albino	Control	Albino	Control	Albino
Pair 1	Normal	Esotropia 45° alternating; motility severely restricted and confined to medial direction; head erect; nystagmus	PERLA	React to light but not to accommodation	Brown	Grey blue Typical albino
Pair 2	Normal	Esotropia 10° alternating, no restriction of motility; head erect; slight nystagmus	PERLA	PERLA	Brown	Grey blue Typical albino
Pair 3	Normal	Esotropia 45° alternating; motility severely restricted and confined to medial direction; head tilted and face turned to right; nystagmus	PERLA	Pupils react to light but not to accommodation	Brown	Grey blue Typical albino
Pair 4	OD Normal OS Corneal opacity with anterior synechia	Esotropia 45° alternating; motility severely restricted in lateral field of gaze and somewhat restricted in superior and inferior movement; head tilt to right; nystagmus	Reflexes intact OS oval shaped	Pupils react to light but not to accommodation	Brown	Grey blue Typical albino
Pair 5	OD Cataract and anterior synechia OS Normal	Esotropia 10°-20° alternating; motility somewhat restricted superior and temporal movement; head tilt to right; nystagmus	Reflexes intact; OD oval shaped	Pupils react to light; accommodation questionable	Brown	Grey blue Typical albino
Pair 6	OD Small Pterygium OS Normal	Esotropia 30°-45° left eye fixing; motility restricted in superior and temporal movement; head erect, moderate nystagmus	PERLA	OD—No direct pupil reflex. OS—Reacts to light but not to accommodation	Brown	Grey blue Typical albino

TABLE 2

	Media		Fundi		Ocular Pressure		Color Vision	
	Control	Albino	Control	Albino	Control	Albino	Control	Albino
Pair 1	Clear	Clear	Normal	Typical Albino	17.3/14.6	12.2/12.2	Normal	Normal
Pair 2	Clear	Clear	Normal	Typical Albino	17.3/17.3	14.6/12.2	Normal	Normal
Pair 3	Clear	Clear	Darkly pigmented lesion in macular area resembling old lesion of toxoplasmosis	Typical Albino	10.2/10.2	20.6/20.6	Normal	Normal
Pair 4	OD Clear OS Corneal opacity and anterior synechia	Clear	Normal	Typical Albino	10.2/10.2	14.6/17.3	Normal	Normal
Pair 5	OD Cataract and anterior synechia OS Clear	Clear	OD not observed OS Normal	Typical Albino	12.2/14.6	14.6/14.6	Normal	Normal
Pair 6	Clear	OD subluxation and partial absorption of lens OS Clear	Normal	OD Pale grey, possible flat detachment of retina OS Typical Albino	14.6/12.2	14.6/17.3	Normal	Severe red green defect; medium yellow blue defect

TABLE 3

REFRACTIVE ERROR

	Control			Age		Albino		
	Acuity	Refraction	Acuity			Acuity	Refraction	Acuity
Pair 1	OD 20/25	+0.50 ⊂ −1.25x90	20/20	33	36	10/400	−21.00 ⊂ −5.00x20	20/400
	OS 20/25	+0.75 ⊂ −1.25x90	20/20			10/400	−19.00 ⊂ D. sphere	20/400
Pair 2	OD 20/20	+0.25 ⊂ −0.25x90	20/20	21	26	20/400	−2.00 ⊂ −3.00x45	20/200
	OS 20/20	+0.25 D. sphere	20/20			20/400	−5.00 ⊂ −3.00x135	20/200
Pair 3	OD 20/200	−0.25 ⊂ −0.50x180	20/200	26	29	20/400	−3.00 ⊂ −5.00x180	20/200
	OS 20/20	Plano	20/20			20/400	Plano ⊂ −6.00x170	20/200
Pair 4	OD 20/20	+0.25 ⊂ −0.25x180	20/20	24	22	5/400	−14.00 ⊂ −1.50x180	20/200
	OS 20/200	Corneal Opacity	20/200			5/400	−12.50 ⊂ −0.75x180	20/200
Pair 5	OD L.P.	Cataract	L.P.	22	21	20/400	−6.00 D. sphere	20/200
	OS 20/20	+0.25 D. sphere	20/20			20/400	−3.50 ⊂ −1.00x90	20/200
Pair 6	OD 20/40	−0.75 ⊂ −0.75x90	20/25	34	35	Blind	+11.00 ⊂ −2.00x180	Blind
	OS 20/25	Plano ⊂ −0.75x90	20/20			10/400	−5.00 ⊂ −6.00x180	20/200

tribal leaders are aware of their physical handicaps and usually assign duties commensurate with their physical abilities.

In three cases the external examination revealed no head tilting or face turning to compensate for the strabismus. Subsequent examination of photographs makes this finding subject to doubt. These photographs reveal varying degrees of tilting or turning in all cases. The erect position may have been assumed in an effort to aid in the eye examination.

Ocular motility was restricted in all of the albinos except the albino in Pair 2. This man was better developed physically and engaged in daily calisthenics. He had a lower degree of esotropia but all of the other findings were consistent with the albinos as a group. In the other five albinos there appeared to be a paralysis of both lateral rectus muscles.

Nystagmus was present in all cases and was of the ocular or fixation type with lateral movement of varying intensity. At the time of examination this was reported to occur in the Moon-children at birth before foveal fixation could possibly be attempted. This led to some speculation and question about neurological defects. However, it has since been reported to C.E.K. by a Cuna woman having four albino children, that the nystagmus begins at about the age of one month. Photophobia was present but was of little concern to the albinos. They accepted it as a nuisance and had adjusted to this defect.

The albino iris is of a light grey blue color with a brown pigment ring in the pupillary area and with radiating brown streaks in the ciliary area. This is contrasted with the rich chocolate brown of the control group. Transillumination of the globe caused the albino iris to take on a typical pink glow. Slit-lamp examination revealed a pale blue (with brown previously noted) iris which appeared to be thin and gave the illusion that one could almost see through it. The fundi of the six Moon-children were all typically albino with chroidal vessels seen clearly. Patches of white sclera were visible between the vessels, with a more red area where the macula would normally be located. In no case was a normal macular area observed. The optic nerve head was visualized in all cases, but appeared clearer in some due to the nature of the refractive errors and the nystagmus.

One albino was found to have a severe color vision defect. The test used was A.O. H-R-R Pseudoisochromatic Plates, 1957 Edition. The nature of the refractive errors caused the albinos to hold the charts about six inches from the eyes. Those having normal color vision appeared to have no difficulty seeing the characters.

All six of the albinos were severely myopic. This appears to be

true for all Moon-child albinos observed in San Blas during fourteen years. Thus an elongated eye ball may be a characteristic manifestation of the albino gene. Six of the albino eyes showed astigmatism of more than three diopters.

It now appears that a measurement of corneal curvature should have been attempted. This would be quite difficult in the case of the albinos because of the esotropia and nystagmus. If future studies are made possible this test will be included.

A spectacle correction was provided for each of the albinos in a number two green tint. Two of these corrections were in the myodisk form. Fonda[8] reports using a high bifocal correction to improve near visual acuity. This idea was first considered and later discarded because of the nature of the Cuna culture and expected difficulties with the initial single vision prescription. As might be expected from the strength of the corrections, some initial difficulties with depth perception were inevitable. It was observed that all of the albinos had some problem with walking, eating and distance appreciation. However, by the time they departed from Milledgeville State Hospital they all appeared to have overcome their initial difficulties. It is hoped that these spectacles will be worn and to a certain extent improve the lives of these people. It is possible that the spectacles may assume the proportions of a status symbol thus assuring their continued wear.

SUMMARY AND CONCLUSIONS

The visual findings of six albino Indians were compared with normally pigmented controls from their own tribe. All of the albinos were classified as having complete generalized albinism. Photophobia, myopia, nystagmus and esotropia were constant in the albino group. In two cases the myopia was exceptionally high. The nystagmus was of the fixation or ocular type. Ocular motility was severely restricted in all but one albino. The albino iris is a grey blue color with some brown pigment.

Future studies are indicated to determine if myopia is a characteristic manifestation of the albino gene. This should include albinos in a younger age group. More information is needed on the age of onset of the nystagmus. Future studies should include an attempt to measure corneal curvature.

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THE INCIDENCE OF CUNA MOON-CHILD ALBINOS

CLYDE KEELER*

SEVERAL authors have attempted to count the albinos in the Caribe Cuna Indian population of San Blas Province, Panama[1-5]. Each has been amazed at their high incidence, but little has been offered by way of explanation for such a concentration of albinism. (The Cuna call them "Moon-children" and believe they are caused by either the mother or father looking at the moon too much during gestation.) Probably no account is highly accurate, because of certain difficulties that will be discussed in this paper, but estimates can be sufficiently precise to warrant a few conclusions.

Such counts have usually been made by visiting the larger, more civilized islands, recording the albinos there, and then, through inquiry, learning of the presence of albinos on other islands. I have visited the coast that includes the inhabited islands from Mandinga to Titumate. Reports on the few hostile mountain towns had to be obtained from traveling residents of those towns.

Wafer, the pirate, (ca 1681) estimated that the incidence of albinism among the Cunas was 0.3 to 0.5 percent, or 30 to 50 per 10,000 population[5] (Table I). This estimate has been followed by the work of Harris[1], Stout[4] and Keeler[2].

It will be noted in Table I that Stout[4] recorded fewer albinos than did Harris or Keeler. Stout accounts for this by assuming that his own figures are more accurate than those of his predecessor, Harris. However, from the consistency of Harris's 1925 studies with mine of 1950 and 1962—where the incidences are 69/10,000, 67/10,000 and 61/10,000 respectively—it would appear that Stout was probably the one in error and Harris's estimates were fairly accurate.

TABLE I. Estimates of Cuna Indian populations and albinism

Author	Date	Total population	No. of albinos	Albinos per 10,000 population
Wafer	1681	?	?	30–50
Harris	1925	20,100	138	69
Stout	1940	20,831	98	47
Keeler	1950	22,822	152	67
Keeler	1962	23,743	144	61

Infanticide

The practice of infanticide complicates the problem. Supreme Chief Nele Kantule, a prestigous leader of the Cunas, actively and constantly preached to the Cunas during his rule that because the albinos sin less than other Indians, they are on better terms with Tiolele, the Sungod, and for this reason they should not be killed at birth, but should be kept alive so that they might tell the Cunas more about God.

Before the time of Nele Kantule the percentage of albinos kept alive was probably much lower than during his rule, as suggested by the incidence estimated by Wafer.

Following his death, however, the incidence of albinos seems to have declined outside of the large and more civilized towns, and various Indians tell me that there is now a considerable amount of infanticide, especially on the smaller, less civilized islands. This recently increased practice of infanticide would help to account for the drop from 67 per 10,000 in 1950 to 61 per 10,000 in 1962.

Although we expect to find some variation in the albino gene distribution on different islands, we may check our assumption of infanticide by comparing the incidence of albinism in 1962 for

* Milledgeville State Hospital, Milledgeville, Georgia. This paper was presented at the Meeting of the American Academy on Mental Retardation at the Kennedy Child Research Center, April 6, 1963.



CUNA ALBINOS

Figure 8

Cuna albino boy showing infected mosquito bites and Cuna woman and man showing squamous cell carcinoma. Infections and the metastases of skin cancer are chief causes of reduced viability in Cuna Moon-children.

more civilized Cuna towns with that of less civilized towns.

The data from the more highly civilized towns—Ustuppo, Ailigandi, Mulatuppo, Nargana, Corazon de Jesus (Nusatup) and Ignacio de Tupile—where the killing of newborn children is frowned upon, show a high rate of albinism (Table IIA). Among these towns a population of 6,365 persons includes 92 albinos, or 144 per 10,000. Nargana, the town that has been transformed most by changing acculturation, shows the astounding rate of 475 albinos per 10,000 population.

We note that the albino incidence is not as high in a group of the larger towns that are considered to be less civilized than those above (Table IIB). Among the 2,594 persons in less civilized towns we find 14 albinos, or 54 per 10,000.

Thus, there is more than twice the incidence of albinos in the more civilized large towns than in the smaller, less civilized ones.

Figures for the uncivilized small towns and islands where only a few families were present, where infanticide could be hidden easily, and where there was little or no social pressure against this time-honored custom, show an even more striking reduction in the incidence of albinism (Table IIC). The 68 other Cuna localities, ranging from 3 to 746 inhabitants, as recorded in the 1960 census, have 33 albinos in a total population of 10,411, or 32 per 10,000. Thus, the statements of various Indians that infanticide is practiced on newborn albinos, especially in the small villages, is substantiated by the data collected.

The small, uncivilized localities have more than four times fewer albinos than the large, more civilized towns, and almost 60 percent fewer than in the quasi-civilized large towns.

It will be noted that the figure 32/10,000 is actually near the lower limit of Wafer's estimate of 30 to 50 per 10,000 for the uncivilized Cunas of his day.

Absentees and Census Records

Aside from the practice of infanticide, the method of recording the censuses taken by the Panamanian Government is a second factor that distorts the observed incidence of albinism among the Cunas. Official census records do not include as Cunas any members of the tribe who may have found employment outside the Reservation. They are recorded as Panamanians.

In 1925, Harris[1] had to estimate the

TABLE II. Incidence of albinism in towns selected as civilized, less civilized and uncivilized

Name of town	Population	Number of Moon-children	Incidence per 10,000
A. Civilized:			
Ustuppo	1,705	8	40
Mulatuppo	1,383	14	101
Ailigandi	1,355	24	177
Tupile	868	8	92
Nargana	632	30	475
Corazon de Jesus	423	8	189
Total	6,365	92	144
B. Less civilized:			
Playon Chico (Okup Seni	1,178	5	42
Achutuppu	781	6	76
Mammituppu	635	3	47
Total	2,594	14	54
C. Uncivilized:			
68 localities ranging in size of population from 3–746	10,411	33	32

population of San Blas, as there was no census report available to him at that time. In 1940, Stout[4] added 4,000 working absentees from the Reservation to the 1940 census population record for San Blas.

In 1950, in order to adjust the population figures of the census, Dr. Alcibiades Iglesias (an educated Cuna) and I estimated, on the basis of the number of Cunas seen on the streets of Colon and the City of Panama, that there were then 2,000 absentees from the Reservation. In 1960, Iglesias and I estimated that the number of absentees had increased to 4,000. However, the number of absentees varies from time to time.

For 1962, I have taken the 1960 census figure, added 4,000 for absentees, and an additional 400 for normal population increase.

It is felt that Stout's estimate[4] of 4,000 absentees may have been too high, since his number of albinos is definitely too low when compared with the figures of Harris[1] and Keeler[2].

Stout compared his 1940 data on the percentage of albinos for several towns with the 1925 data of Harris. We continue this comparison for 1950 and 1962 in Table III.

All towns except Nargana seem to hold their incidence of albinism at a constant number. Albinism in Nargana, however, has steadily increased, although its population is now about one-half of what it was in 1925.

Viability

The old men say that albinos, on the average, do not live as long as normally-pigmented Cunas[1]. Indeed, Chief Lacenta told this to Pirate Wafer almost 300 years ago. The validity of this belief may be examined statistically. Out of 156 normal Indians whose ages were recorded, 51 or 32.7 percent survived to 40 years of age, according to census data. Out of 74 albinos whose ages were recorded, four or 5.4 percent survived to 40 years of age. Taking the 32.7 percent as normal, the albinos have a survival value of 16.5 percent of normal at age 40. The breakdown shows that 117 normal females had a mean age of 22.5± 1.5 years and 197 normal males had a mean age of 21± 1.1 years. From our 1962 data we learn that 26 albino females have a mean age of 18.0± 1.6 years, and 48 albino males have a mean age of 16.3± 1.6 years.

Several factors are involved in the

TABLE III. Incidence of albinism in specific towns over the years

	Harris 1925			Stout 1940			Keeler 1950			Keeler 1962		
	No. of albinos	Pop.	Albinos per 10,000	No. of albinos	Pop.	Albinos per 10,000	No. of albinos	Pop.	Albinos per 10,000	No. of albinos	Pop.	Albinos per 10,000
Ailigandi*	12	1250	96	14	605	231	21	1218	172	24	1354	177
Ustupo	5	1000	50	4	1139	35	8	1356	59	8	1705	47
Nargana	8	1200	67	12	1029	166	24	608	394	30	632	475
Tupile	2	250	80	4	622	64	10	752	133	8	868	92
Plyon Chico	2	300	67	2	576	26	2	902	22	5	1178	42
Tigre	2	150	133	4	573	70	3	550	54	4	671	60

* Population figures for these towns were given upon request by the Panamanian Census Bureau and differ somewhat from their published figures.

TABLE IV. Calculations from the Cuna pedigree data, by year

Date	Total pedigree population	Albinos calculated	Albinos found	χ^2	Probability
1950	269	95.291	103	0.694	.30 – .50
1960	286	103.581	96	0.870	.30
1962	269	102.327	111	1.186	.05 – .30

Cuna sex-specific death rates. According to our records, females enjoy a more protected life than males, thus achieving a greater age. On the other hand, it is estimated that one-third of Cuna girls, on the average, will die in childbirth, a factor tending to reduce the mean age of the girls.

It will be seen that the mean age for albino females is 18 years compared with 22.5 years for normal females, although the difference may not be statisistically significant.

Albinos seldom marry, although a few albino girls are married and others have illegitimate children. The rareness of childbearing extends the mean age of those albino girls that reach a reproductive age. All albino girls lead sheltered lives, compared with normal girls.

The normal boys are subject to environment hazards, such as poisonous plants and animals, and occupational accidents. The albino boys are somewhat protected, and their reduced mean age is evidence of their reduced viability.

Gene Frequency

The data collected in 1950 and 1962 show a decline of the actual number of albinos during the past 12 years. The frequency has declined from 67/10,000 to 61/10,000. (Chief Nele Kantule, who preached against infanticide, died in 1944.) However, considering the results of complete selection at the end of one generation, with the albinos excluded from the mating pool, and without mutation, we may calculate from the formula

$$q_1 = q_0/(1 + q_0), \qquad (1)$$

an expected frequency of 57/10,000 for the succeeding generation instead of the 61/10,000 that we found. Assuming 18 years between generations (since the average female is dead at 22) the incidence in 1940 should have been over 67 and that in 1925 should have been over 82.5; or, calculating in the other direction, we have too many albinos today, according to the calculated mutation rate. Nevertheless, it is unsafe to press these conclusions too far because of the necessity of estimating absentees, although we feel relatively certain that nearly all of the albinos have been counted.

Mutation Rate

By use of the formula $M = f(1 - F)$ it may be calculated that something in the neighborhood of 398 mutations to Moon-child albinism are added to the gene pool per 10,000 each generation of about 18 years duration. This would result in about five new albino homozygotes per generation in order to keep the incidence at equilibrium.

However, according to the formula (1), in the two generations between 1925 and 1962 there should be a greater reduction in the incidence of albinism than was observed.

While we may have indications and hunches from the mathematical treatment of our data, we dare not draw absolute conclusions because of the estimated approximations that cannot be determined precisely such as: 1) number of absentee workers, 2) number of siblings, 3) number of infanticides, 4) number of years between generations, and 5) exact ages of older persons for whom the date of birth was not recorded.

The 3:1 Ratio

My 1950 calculations[2] from the pedigree date, using the formula

$$aa = .25/[1-(.75)^n]$$

to adjust for the Hardy-Weinberg law, may be compared with my 1960 and 1962 data and calculations (Table IV). It will be noted that in 1960 there were fewer albinos than calculated but that in 1950 and 1962 there were more than expected. However, in spite of the tendency to eliminate some albinos today, we have more albinos in the pedigree data than expected on the basis of a 3:1 ratio. This may be partly due to the psychological tendency of informants to remember the affected persons in a sibship but to forget the normal siblings.

Summary

The incidence of Cuna Indian Moon-child albinos is more than 60 per 10,000 population, being reduced from about 69 per 10,000 in 1925. Stout's 1940 estimate of 47 per 10,000 is probably in serious error. Our 1962 data suggest infanticide in uncivilized towns and possibly selective interbreeding of heterozygotes in the town of Nargana. Absolute population figures cannot be obtained, due to census methods and unrecorded absentees. Our figures show albinos to be less viable than normals, in keeping with general Cuna belief. Since albinos seldom reproduce, the gene frequency in one generation without mutation should have been reduced to 57 per 10,000, so there is evidence that mutation does take place. It is estimated that about 398 mutations per generation per 10,000 population are added to the gene pool in order to provide the five albino homozygotes per generation necessary to keep the incidence at equilibrium. Examination of the 1950, 1960 and 1962 data all show Moon-child albinism to be due to a single pair of recessive, Mendelian, mutant genes.

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A COMPARISON OF THE INTELLIGENCE AND PERSONALITY OF MOON-CHILD ALBINO AND CONTROL CUNA INDIANS* [1]

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A. INTRODUCTION

Albinism is a simple, recessive Mendelian characteristic. Several studies have investigated the albino for evidence of significant psychological differences that may exist as the result of a structural change. A review of the literature indicates that there are two relevant studies on the psychological aspects of albinism. Segers (3) wrote a monograph based on the examination of one albino child. He concluded that the albino showed intellectual retardation, emotional instability, and a tendency toward combativeness. In the Chicago schools, Beckham (1) studied 42 Negro boys and girls who were albinos. He found that there were some general findings that applied to the group. They exhibited a general feeling of insecurity, apparently due to their maltreatment at home, as well as by society, because of the stigma of being different. He found the usual visual difficulties, but more generally he reported that physical development was retarded, as evidenced by slowness in walking and talking. He did not detect any significant difference in the intelligence of the albinos when compared with their nonalbino siblings. Finally, he concluded that the albino child should be given psychological counseling to help him overcome the difficulties brought on by being different.

In the present study, albino and nonalbino Cuna Indians were compared on the basis of their responses to psychological tests. The primary problem was to determine if there was a difference in the intellectual ability of these two groups of Indians. The social stigma of albinism is minimized in Cuna society. A second line of investigation was to determine if there were any salient personality differences between the two groups. On the basis of the experience of one the authors (Keeler), differences in personality were expected, whereas differences in intelligence were not. Keeler (2) has reported that there are

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definite differences in the child-rearing and adult experiences of albinos among the Cuna.

B. Method

1. *Subjects*

The subjects for this study were 12 male San Blas Cuna Indians. They were flown to the Milledgeville State Hospital from their native Panama for a two-week examination. The albinos averaged two years older, with the range of age for the albino and control subjects being from 22 to 36 years. The controls had a little more formal education, with the modal amount of education for both the albinos and controls being approximately the sixth grade. The controls tended to have more contact with civilization. Only one Indian, a control, was married.

2. *Test Conditions*

In general, the testing conditions were not optimal. The Indians were undergoing extensive medical tests and examinations in a strange country. Rapport dwindled during the second week of the examination period. All psychological testing that required a verbal response was performed by a Spanish-speaking psychological intern who was a native Cuban because Spanish is the official language of San Blas. Of the entire group of Indians, only one Indian (an albino), could not speak Spanish adequately. It was found that more than the usual amount of pretest instructions were needed to orient the Indians to the tests.

3. *Test Procedure*

Psychological testing was performed while the subjects were awaiting various medical examinations. They were first given the intelligence test battery: the Draw-A-Person test; the IPAT Culture Free test of "g," Scale 2; three subtests from the Wechsler Adult Intelligence Scale (arithmetic, similarities, and block design); and the Arthur Adaptation of the International Performance Scale, Tray 2. When this entire battery had been administered, each subject was given individually the Rorschach Psychodiagnostic Test. The lack of sufficient time precluded further personality assessment.

In addition to the formal scores obtained in the various psychological tests, the entire battery of tests were submitted to five clinical psychologists at the doctoral level for rating the subjects as to their relative psychological health. These judges attained a Kendall coefficient of concordance of .76 in ranking the subjects on the test battery without the Rorschach. One of the authors

(Stewart) interpreted the protocols of the two albinos and two controls who had the highest rank in psychological health for general personality trends.

For a determination of the statistical significance, nonparametric tests were used. The Mann-Whitney U test was employed to determine the significance of the differences obtained on the intelligence tests. The correlations were based on the Spearman rank difference method.

C. Results

There were no conclusive differences obtained in the intellectual ability of the albinos when compared with the controls. An intelligence quotient obtained by prorating the three subtests of the Wechsler Adult Intelligence Scale was used as the most valid indication of intelligence. The average IQ score for the albino was 80, while the average IQ for the control was 86. This difference was not found to be statistically significant ($p = 0.29$). The range of IQ scores for the albinos was from 58 to 100, while the range for the controls was from 71 to 93. Table 1 presents the data for the IQs obtained, while

TABLE 1
*IQ*s and the Intelligence Tests Administered to Controls and Albinos

Subject	IPAT g	WAIS	Arthur Scale
	Controls		
Morales	23	71	67+*
Benitez	63	84	69
Assa	78	91	81+
Perez	78	89	71+
Rivera	31	93	77+
Martinez	70	89	77+
	Albinos		
Diaz	23	71	50
Rossi	—	58	50
Lloyd	58	84	63
Pena	63	100	70
Miseli	50	74	52
Avila	61	93	56

* A plus sign signifies that the subject could have done better if the next step of the scale had been available.

Table 2 gives the rank order correlations between the various intelligence measures.

There was one intelligence test that yielded a significant difference in the performance of the albinos and the controls. The Arthur Adaptation of the International Performance Scale gave a statistical significance ($p = .004$).

This was discounted as it appeared to be largely dependent upon the poor vision of the albino. The uncorrected visual acuity of the albinos ranged from 5/400 to 20/400. These subjects were tested before their vision was corrected. Corrected vision was 20/200 for four of the albinos, while one had a corrected

TABLE 2
THE RANK-DIFFERENCE CORRELATION OF THE INTELLIGENCE TESTS USED
DECIMAL POINTS ARE OMITTED

IPAT *g*	Block design	Similarities	Arithmetic	WAIS *IQ*	Arthur
IPAT *g*	74	60	28	63	72
Block design		33	42	65	59
Similarities			24	82	74
Arithmetic				68	27
WAIS *IQ*					67

vision of 20/400. Therefore, it was concluded that (for the subjects used) there was no demonstrable difference in the intellectual ability between the albinos and controls.

In general, the results on the different intelligence tests tended to agree with each other. A Kendall coefficient of concordance yielded a value of .54 ($p < .001$) for the agreement between the IPAT "g," the subtests and the total score of the WAIS, and the Arthur scale.

The general psychological health of the two groups was obtained through summing the five independent rankings by the judges on each subject. The results of this ranking are presented in Table 3. Psychological health was found to correlate .61 with the subject's intellectual ranking. The order of

TABLE 3
THE SUMMED RANK ORDER OF SUBJECTS IN TERMS OF THEIR PSYCHOLOGICAL
HEALTH AS JUDGED BY FIVE JUDGES

Subject	Experimental condition	Psychological health rank	WAIS *IQ*
Ossa	control	1.0	91
Perez	control	2.0	89
Martinez	control	3.0	89
Pena	albino	4.0	100
Lloyd	albino	5.0	84
Avila	albino	6.0	93
Morales	control	7.5	71
Benitez	control	7.5	84
Rivera	control	9.0	93
Miselis	albino	10.0	74
Rossi	albino	11.0	58
Diaz	albino	12.0	71

the ranking indicates that the controls were rated as being psychologically more healthy than were the albinos.

A comparison of the two albino and two control protocols that were ranked highest in each group on psychological health reveals a basic difference in the level of emotional development and the use of defense mechanisms. The control group showed a more striking masculine identification. They were more alert in the testing situation, made a better adjustment to the personnel, and were more willing to try new things. Communication was easier with them, and they were freer in the expression of their ideas. In general, they were direct in the manifestation of their feelings, could show anger and hostility, and were actively interested in the opposite sex.

On the other hand, the albinos revealed a passive, dependent, feminine orientation. They showed little active interest in the opposite sex, tending to relate to females on a prepubertal psychosexual level. The albinos were more anxious and insecure, and they relied heavily on several defense mechanisms to allay their anxiety. Some showed a definite religious orientation, while others attempted to intellectualize their anxiety. These two personality defenses are actively fostered by the tribal culture which accords the albino status in religious activities and offers outlets in intellectual pursuits. The third pronounced defense mechanism is denial, which is also heavily sanctioned by the tribe. The albinos tend to deny that there is any difference between themselves and the controls. This denial tends to break down under moderate stress, leading to hostile, resentful, and angry responses. Often withdrawal is resorted to when the denial breaks down. In general, the albino shows a markedly less accurate perception of reality.

A comparison of the albino and control Indians shows that the albino is more immature emotionally. It is difficult to find the cause of this immaturity. It may be due simply to the early parental overprotection or to the inheritance of a poorer basic personality. An interaction between both factors is likely. The pattern of emotional instability was fairly constant for all six albinos tested. As Table 3 shows, even the most healthy albinos are not rated at the same level as are the most healthy controls.

D. Discussion

This was a study of the intelligence and personality of six albino and six brown control San Blas Indians. There is an essential agreement with Beckham's findings. A significant difference in intelligence could not be demonstrated when the albinos were compared with controls of the same tribe. The

albinos showed the greatest range of *IQ* scores, while the average *IQ* was higher for the controls. There was no evidence to support Seger's findings that mental retardation is related to albinism, if moon-child albinism is genetically identical with the albinism common to other populations.

Some personality differences were obtained, indicating that the albinos were less emotionally stable and more immature than were the controls. These findings cannot be unequivocably argued as being the product of either nature or nuture. Apparently, some findings can be related to environment, while others are more in keeping with a genetic explanation.

The present study tends to confirm the findings of Beckham and some of those of Seger. The results need further confirmation with a larger sample and with subjects who are not simultaneously undergoing stressful medical tests.

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THE CUNA MOON-CHILD SYNDROME

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In 1941 we showed that the melanotic form of the wild gray Norway rat, the piebald condition and albinism are not isolated genetic entities, but rather that each is the external indicator of a unique syndrome of modifications of glands, sense organs and brain,[1] determining specific alterations in physiology which, in turn, modify behavior.[2] If these three coat-color genes are all present in the same individual, their pleiotropic modifications are additive and largely account for all the physical, physiologic and behavioristic modifications found in the tame Wistar albino rat.[3] The summated physical and physiologic effects of these three coat-color genes plus the effects of any other unlabeled taming genes that have mutated in the Wistar or related tame stocks and have become homozygous constitute the "marks of domestication" written about by Darwin, and identified anatomically, physiologically or behavioristically in the rat by such investigators as H. H. Donaldson,[4] J. C. Donaldson,[5] Keeler and King,[1] Rogers and Richter,[6] Fish and Richter,[7] Griffiths,[8] Richter,[9] Stone,[10] Hall,[11] Farris and Yeakel,[12] and others.

All these researchers except Keeler and King had the disadvantage of not knowing how many unidentifiable genes making for physical modification, and thereby for greater tameness, had mutated in their tame stocks that reduced the wild manifestations of their gray coat-color animals in the F_2 and the Norway-Wistar hybrids backcrossed to their Wistar parents. Keeler and King studied not only the F_2 of a Norway-Wistar cross but they also investigated the coat-color mutants that cropped out after the 12th generation of captive gray Norways, with the advantage that their results are clear-cut and not weakened by the presence of unlabeled taming genes.

The studies of Keeler and co-workers have shown that these mutant coat-color genes themselves are the causes of whole syndromes of unique pleiotropic modifications of glands, sense organs and brain. The study of pigment gene pleiotropia has been extended from rats to both mink and

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foxes. It has been explored in man in albinos[13] and redheads,[14] where it finds medical applications.

Because of the implications for psychology, psychiatry and medicine, it was decided to study as many as possible of the 144 Cuna Indian Moon-Children whom we registered in San Blas Province, Panama. The assumption was that the Moon-Children are the result of an albinistic syndrome like the coat-color syndromes of rats, mink and foxes, and not just lacking pigment. The fact that the Moon-Children are all from the same small tribe of 23,000 persons gives the advantage of uniformity of residual hereditary background, upon which the characteristics of the syndrome will stand out more sharply than in albinos culled from heterogeneous stock, as would be the case if we studied albinos in the United States.

We are particularly interested in problems of mental retardation as well as in the psychologic and psychiatric aspects of these studies. We are interested in any deviations in morphology and physiology, especially those which might contribute to changes in behavior. It is common belief that albinos tend to be mentally retarded, but there are brilliant exceptions presenting a problem that we would like to elucidate. We are concerned with producing a détailed description of the Moon-Child Syndrome.

A large team of specialists cooperated in this research program: Donald Moyer, M.C., U.S.A., dermatologist; Joseph Bohorfoush, cardiologist and hematologist; Serio Alvarez-Mena, cardiologist; Reichart Johnson, dentist; George Courtney, optometrist; Horace Stewart, psychologist; Virginia Balbona, intern in psychology; Helen Pessino, radiologist; Walter Bowman, laboratory specialist; Lillas James, medical geneticist; Julian Gomez, psychiatrist; Hosea Balbona, psychiatrist; José G. Mendosa, psychiatrist; Joaquin Piedra, psychiatrist; Carlos Maruri, psychiatrist; Herbert Goldsmith, music therapist; Becky Fuller, laboratory technician; Penny Edwards, tissue culturist; Virendra Mahesh, biochemist; Herman Dominguez, tissue culturist, and José Rauco, otolaryngologist.



Fig. 1—Mother and child—Cuna Indian albinos (photograph courtesy of Dr. Edward Cleve, Division of Tropical Medicine, Tulane University of Louisiana School of Medicine).

Examinations

After a cursory examination of 35 Moon-Child albinos on the San Blas coast, carried out by Moyer and Keeler, six albino males ranging in age from 21 to 36 years, together with paired brown-skinned controls of the same age and sex, were brought to the Milledgeville State Hospital for two weeks of intensive study. Each member of the team was responsible for the examinations in his own specialty.

Anthropometrics

Measurements were recorded for weight, height, chest circumference (inhale and exhale), wrist circumference, length of tibia, length of femur plus tibia, metacarpal dimensions, head circumference, parietal diameter of head, fronto-occipital diameter of head, facial length, nasal length and manuometer deflections. The results showed the over-all body size of the albinos to be smaller than that of the controls rather than changed in bodily proportions. However, the greater mean of length of the albino nose becomes statistically significant when expressed as a function of facial length, indicating that the albino nose is, in contrast, proportionately longer than the brown-skinned one; a study of the figures for the third metacarpal indicates that the albino shaft is proportionately narrower.

It is interesting that mutant albino mink, rats and other mammals are smaller than normals, and that in rats the amount of reduction in body weight and body length is almost identical to that in Moon-Children.

Skeleton

The bones of Moon-Children tend to be more gracile than those of controls, as shown by our x-ray studies. The Moon-Child skull tends to be brachycephalic. Observation of many Moon-Children on the San Blas coast resulted in the impression that the malar eminences do not protrude as much as those of brown skins. X-rays taken in the Walter position show a more narrow nasal region and the malar eminences actually farther in from the lateral periphery of the skull.

The forehead shape of Moon-Children is typical and differs from the normal. In profile there is a more gradual slope to the Moon-Child forehead. The teeth protrude less and the point of the jaw tends to be more sharp than in the controls.

The cartilage elements of Moon-Children are affected. How much of this may be due to the tropical sun we do not know. Not only is the nose of Moon-Children elongated due to cartilage hypertrophy, but the ears flare and cup due to cartilage overgrowth, while there develops a row of nodularities along the brim of the superior auricular cartilage. It is probable that in some Moon-Children the cartilages of the throat are somewhat hypertrophied because two out of six had a throat aperture so small that the vocal cords could not be visualized with a speculum. One of these, and probably both, had trouble swallowing. Chest shapes of Moon-Children tend to be abnormal.

Skin, Hair and Cancer

The scalp hair of albinos is invariably finer than that of controls. In childhood, hair may be found at the sides of the face and always on the distal segments of the limbs.

Just as the eye color may darken with age so may the scalp hair, changing from white to yellow and, in some cases, to red and even to brown. This change is probably enhanced by the intense tropical sunshine. The skin of the Moon-Child infant is pink, softened by short, white hair all over the body. The skin appears extremely thin because capillaries are often evident. As the child grows older he becomes exposed to sunshine and huge freckles appear. Boys become blistered and often carry a number of infected sunburn lesions simultaneously.[15] Further exposure causes hypertrophy of the skin, except under the freckles sunken below the general hypertrophied surface. In this hypertrophied skin one notices seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas. The skin of the girls is much more protected than that of the boys and, accordingly, our statistics show that the Cuna Moon-Child males die younger on the average than the females.

Thirty-five albino Indians were examined in Panama for presence of skin abnormalities, and their severity was graded from 1 to 4+. Factors judged included the number of skin cancers, actinic keratoses, seborrheic keratoses, large freckles, small freckles, nonpigmented nevi and the degree of skin infections. The number of plus marks for identical age groups in both sexes was averaged. These figures present a classic picture of the effects of sun exposure upon skin. There was a gradual increase in the severity of changes in both sexes with age. Although the average age of the males was less than

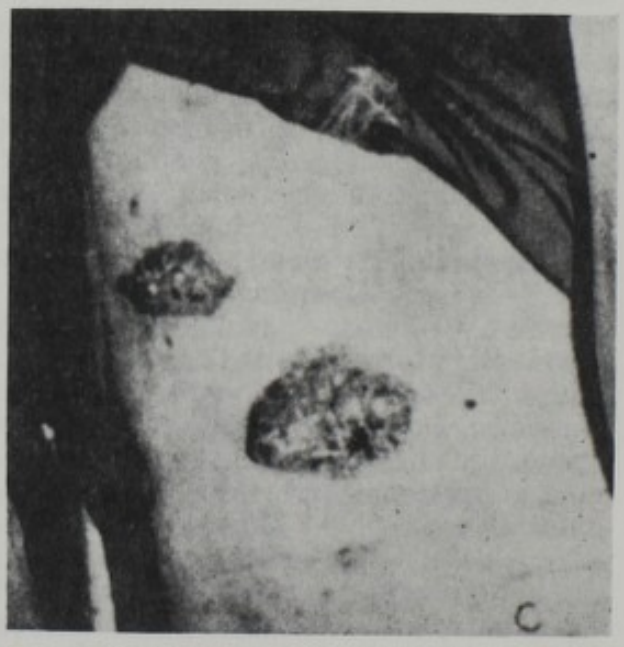


Fig. 2—Cuna albino with squamous cell carcinomata on thorax; lesions were also present on face and arms (photograph courtesy of Dr. Edward Cleve, Division of Tropical Medicine, Tulane University of Louisiana School of Medicine).

that of the females, their skin changes were more severe as their over-all exposure was greater.

The Cunas do not speak of a person after he has been buried, lest this interfere with the journey of his soul in the afterlife. For this reason it is difficult to learn about the cause of death. However, in recent years we were able to determine that among albinistic Moon-Children, if they live to grow up, the chief cause of death is probably metastatic skin cancer.[16] It has been stated by MacFadden that the skin cancers of Moon-Children are squamous cell carcinomas. However, we find from biopsies that although squamous cells composed eight of ten skin cancers, the other two were basal cell carcinomas. Of six Moon-Children brought to the Milledgeville State Hospital, one had a squamous cell carcinoma on the left cheek; two others had squamous cell carcinomas on the right cheek and one on the right shoulder as well as a basal cell lesion on the left temple.

Teeth

The six Moon-Child males and their paired brown controls all had gingival inflammation, calculus formation and other dental defects, and there were no striking differences between the two groups.

One Moon-Child had a malformed tooth, and two had malposition. One albino had supernumerary teeth. However, one control had malposition and one had poor tooth arrangement. Although actually the albinos had more defects, the number of individuals examined were so few that this difference cannot be considered of any importance, especially considering the fact that tooth anomalies are very common in the tribe.

There were 35 decayed teeth among the controls and 36 among the albinos. The teeth do not reflect the weakness shown in the albino skeleton in general, and this is in conflict with reports of sporadic albino mammals found in nature.

Eyes

The fundi of the six Moon-Children were all typically albino with choroidal vessels clearly visible. Patches of the sclera were visible between the vessels and a more red area was observed where the normal macula should be located; in no case was a normal macular area noted. The optic disc was visualized in all cases, but appeared clearer in some, due to the nature of the refractive area.

All the Moon-Children of San Blas show nystagmus of the ocular or fixation type, with lateral movement of varying intensity. The nystagmus does not appear until one month of age, showing that it is a response to light rather than due to a neurologic defect.

All albino irides are blue-gray in color, with a light brown pigmented ring in the pupillary area, and radiate brown streaks in the ciliary area. Transillumination of the eye caused the iris to acquire a typical glow. Slit lamp examination revealed a pale blue iris (with brown as previously noted) which appeared thin and gave the illusion that one could almost see through it. Because of pigment present in hair and eyes, many people deny that Moon-Children are true albinos.

All six albinos were severely myopic. This appeared to be true for all Cuna albinos whom we have examined during the past 14 years. Thus, an elongated eyeball may be characteristic of the Moon-Child Syndrome.

Corneal astigmatism was found in all six Moon-Children examined. Corneal curvature was normal except along the horizontal perimeter which was flattened in five albinos. A similar flattening was noted in the sixth, but in this case, instead of being horizontal in both eyes, the line of flattening was low laterally and high medially. From the standpoint of pigment gene pleiotropia, these constant differences in shape of eyeball and lens curvature are of great importance.

Strabismus was found in all but one (the one with the strongest physique) of the Moon-Children. Three cases were of such long duration that the external lateral muscles could not be made to function.

Vocal Tests

Because we had found an analyzable change in voice to accompany various

coat color mutations in rats,[17] and because Moon-Child voices appeared to be soft and raised in pitch in adult males, we tested the six Moon-Child males and their controls for quality of voice by striking notes on the piano and having the subjects imitate them. Speaking and singing were recorded on tape and again compared.

The tone quality of the Moon-Child voice, both vocal and speaking, appears somewhat lighter and of a higher pitch than that of the brown skins. The vocal range of the albinos was greater than that of the brown skins, but this may be due to the fact the albinos tend to sing more.

It was observed that results obtained from the albinos were better than those from the brown skins. It might be assumed that music is an area that would give ego support to the albino in a field of accomplishment that might accord him some status and recognition within his culture, since he is obviously different from the brown majority and physically weaker.



Fig. 3—Group of Cuna children with one moon child (photograph courtesy of Dr. Edward Cleve, Division of Tropical Medicine, Tulane University of Louisiana School of Medicine).

Laboratory Tests

Three pairs of Indians, albino and control, had the following routine laboratory tests performed: complete blood count, sedimentation rate, sickle cell prep., thymol turbidity, cephalin flocculation, total cholesterol, potassium, sodium, uric H^+, glucose, urea nitrogen, protein-bound iodine, urinalysis, and stool examination for ova and parasites. The others refused to cooperate in these tests, but such refusal will be obviated in the future.

Nothing noteworthy was discovered save that protein-bound iodines were significantly higher in the albinos than in the brown-skinned subjects. Two albinos were in the range of thyrotoxicosis. This is just the opposite of what would have been expected. However, these results are in line with the high basal metabolism figures for the black mutation in rats.[18] Although these tests reveal nothing, it is known that Moon-Children, especially females, mature late.[19]

Special laboratory tests performed in all six albinos and their controls included hemoglobin, serum electrophoresis, urinary acid secretion, Mosenthal's urinary concentration as well as blood typing for the presence of blood group antigens: A, B, O, D, E, C, c, e, Cu^s, F, M, N, S, K, G, Le^a, Le^b, Fa and Di^a. All Indians were O^+. No significant differences were noted between albinos and brown-skinned subjects with respect to other antigens. One of the brown controls was Diego positive, a fact of great importance to anthropologists.

Heart

Out of a sample of 12 Indians, to find, as we did, that five have slight or pronounced cardiac hypertrophy is indeed amazing. In the event that this incidence holds for other samples, the tribe should be studied for hereditary heart defects, which probably exist.

The QRS ventricular pattern of the S1 S2 S3 type is more frequent than the average (in four of five cases) among controls. It was observed but once among albinos. In the albinos there is a tendency to left axis deviation; the tendency in normal controls is to right axis deviation. In the albinos the tendency is for the horizontal position to predominate; in the controls the vertical electrical position predominates. There is no significant change in the rhythm or in the 1-A and 1-1V conduction from both groups.

It will be interesting to note, as further data are collected, whether these are merely chance associations or whether they represent pleiotropic tendencies of the albino gene, in contrast to those of its normal allel.

Intelligence

The six Moon-Children and their brown controls were administered a battery of psychologic tests: Arthur Adaptation of the International Performance Scale (two and one-half to 12 years), I.P.A.T. Culture Free Test of "G", three subtests of the Wechsler Adult Intelligence Scale, Draw-A-Person Test, Bender-Gestalt Visual Motor Test, and Rorschach.

There are several limitations to the interpretation of the test data. First, there is a lack of norms for the Cuna Indians; second, the Moon-Children have extremely poor vision and, third, it was necessary to communicate mostly in Spanish through an interpreter. One of the examiners had Spanish as her mother tongue.

The materials collected were evaluated by five staff psychologists. Where possible, statistical procedures were applied to the data.

The three formal intelligence tests, I.P.A.T. Culture Free Test, Arthur Adaptation of the International Performance Scale and the three selected subtests from the Wechsler Adult Intelligence Test, gave high correlations, indicating that the tests were all approximating the same measure. The three subtests of the Wechsler Adult Intelligence Scale were probably the best measure of intelligence of the two groups compared. Only one intelligence test, the Arthur Adaptation of the International Performance Scale, showed a significant difference between albino and control ($P = .004$). This difference appears significant even on casual inspection. However, the value of the test may be questioned since it depends heavily on vision. The five remaining tests showed no reliable differences between the albino and the control groups.

The conclusion of the I.Q. study is that no significant difference exists between the intelligence of Moon-Children and that of their controls. These conclusions are in keeping with our earlier interpretation, but at variance with the generally accepted view.

A comparison of two of the albinos with two of the controls, both of whom were ranked as high in psychologic health, revealed a basic difference in their level of emotional development and use of defense mechanisms. There was a striking masculine identification in the control group. They were more overt in expressing hostility, were openly aggressive and had an active interest in the opposite sex. On the other hand, the albinos revealed a passive, dependent feminine orientation. They showed little active interest in the opposite sex, and tended to relate to its members on a prepubertal psychosexual level. They exhibited greater anxiety and, typically, used defense mechanisms to ward off this anxiety. Some had a religious orientation while others relied more on intellectualization of their anxiety. Denial was pronounced. These defenses were weak, breaking down quickly under moderate stress and releasing the underlying hostility and aggressiveness or taking the form of withdrawal. Their reality was less accurate than that of the control subjects, being impaired by anxiety and leading to poorly conceived notions.

Psychiatric Examinations

Each albino and his paired control were examined by a Spanish-speaking psychiatrist. He was instructed to look into nine areas of behavior: relations between parents; relations between mother and patient; relations between father and patient; relations between siblings and patient; relations between siblings and parents; sexual development and functioning; social development; relations to women; adaptational responses, and psychosomatic disorders.

From these examinations it would appear that the Moon-Children lead a rather abnormal life, restrained in many activities by their physical condition. Four albinos (three in their late twenties) had had no sex experience whereas two (in their middle thirties), the bandleader of Nargana and the dancing master of Ailigandi, had been able to attract girl friends by their public performance of music and dance; the dancing master started his sex experience at 31 years of age. That at least some of the albinos may be functional as males is shown by the fact that two of them had sperm in

their urine upon laboratory examination; thus, masturbation probably provides sexual adjustment.

One albino (the dancing master) remains at home and makes baskets, whereas another was for years the Secretary-Treasurer of a local Indian store, proving that a less rigorous life is sought by some of them. The town councils are considerate in manual labor demands upon the albinos.

The albinos of this group had had limited social experiences as compared with the controls. Some albinos had never left the San Blas Islands before their trip to Milledgeville, and one had no formal education. However, they all appeared as well adjusted as their brown counterparts with broader experience. Many albinos have strong family ties and lead productive, happy lives. By necessity (inability to stay in the sunshine) their work is generally in an intellectual sphere where overcompensation is usual. Religion serves as a major support for many of them who take a fatalistic view of life and blame their failures on their albinism "which is God's will." Sexual experience is, as a rule, more limited than among the brown-skinned subjects. This may reflect social taboos, social isolation or feelings of inadequacy. The one albino who boasted of sexual relations with 22 women may well have been proving his adequacy to himself. Overcompensation, repression and massive denial are the major defense mechanisms in both groups. There is no difference between the groups in number of personality problems. It is evident that much more data should be collected upon the psychiatric plight of the Moon-Children.

Discussion

The mutant albino rat (not the laboratory albino) is smaller in most respects than the normal gray controls, the male being 97.66% of normal body length, and the female 98.33%. The thyroid is considerably undersized in both sexes. The hypophysis is slightly undersized in both sexes. The suprarenals are much smaller in males, and slightly enlarged in females. The gonads are 91.00% of normal size in males, and about a quarter of that in females. Olfactory bulbs are 92.69% of normal size in males, and 93.03% in females. Such modifications of organs result in slight changes in behavior in rats. They are more tame than wild gray rats and their voices are raised in pitch[17] from 400 cycles/sec. to 2800 cycles/sec. A raising of the pitch of voice was noted in the Moon-Child males studied.

The smaller size of olfactory bulbs in the mutant albino rat would be expected to dull the acuity of the sense of olfaction. Accordingly, it was not surprising that we found evidences of such dulling[2] in our garlic test. Questioning of the Cunas brings the reply that Cuna Moon-Children also have a dulled sense of smell. A complete study should be made to obtain accurate quantitative measurements of this deficiency. The subject of olfaction led to that of bodily odor. Thus, knowing that phenylketonurics and other human mutants with altered hair color have unique odors and knowing that at least one coat color in mice is accompanied by a special odor, we thought it worthwhile to ask about Moon-Children. Mothers of Cuna Moon-Children say that from birth the albinos have a unique, repulsive odor, as though they needed a bath. This odor becomes worse as they grow older; it was evident on the Moon-Child males brought to Milledgeville, even if they had just taken a bath. This is to be interpreted as evidence of an altered biochemical reaction associated with the albino syndrome.

In a study of wildness and tameness in rats, Stone[10] could distinguish the control from the mutant, but he could not find differences in intelligence. In a similar fashion, one can note differences in temperament between the Moon-Children and the brown skins, but no actual difference in intelligence was observed, contrary to common belief. However, the Moon-Children are psychiatrically disturbed by their handicap.

Summary

The general impression of the investigators is that the brown-skinned Cuna controls are much more masculine, and that their muscles are better developed than those of the albinos. This impression is borne out in various ways. The

average weight of the six Moon-Child males studied at the Milledgeville State Hospital was almost 10% less than that of the brown-skinned subjects. The bones of albinos are more gracile and bear less calcium deposit than those of the brown controls.

In chest circumference, head circumference, parietal diameter and fronto-occipital diameter of the head, facial length, mandibular length, nasal length, interorbital length and distance, length of femur plus length of tibia, length of tibia, length of foot, wrist circumference, length of radius, and length of humerus plus length of radius, the brown-skinned controls are larger than the albinos, but the proportions in the latter generally remain relatively normal.

However, the length of the nose of the albino is proportionately greater than that of the controls. The Moon-Child tends to be brachycephalic and there is a more gradual slope to the Moon-Child forehead. The skull bones of the nasal region appear underdeveloped with less protrusion of the teeth. The point of the jaw tends to be more sharp in the albinos.

The albino ears flare more than those of normals. The superior auricular cartilage hypertrophies, hardens and forms nodularities along the peripheral border of the pinna. The nasal cartilage elongates and possibly there is hypertrophy of the throat cartilages.

The hair of albinos is finer than that of the controls. In childhood, hair may be found at the sides of the face and always on the distal segments of the limbs. The hair color may change with age from white through yellow to brown or even to red-brown. The skin develops huge freckles and sunburn lesions. Continued exposure to tropical sunshine causes hypertrophy of the skin, except under the freckles sunken below the general hypertrophied surface. Degeneration takes place in the wrinkles of the skin of the inner surface of the elbow joint. In the hypertrophied skin of the body one notices seborrheic keratoses, solar elastoses, and small potential squamous cell carcinomas.

The eyes of Moon-Children are ordinarily blue-gray with some brown about the pupil, but may occasionally change through various shades to brown. They are all myopic. Lateral nystagmus—slow to fast—develops in albinos at about one month of age. Strabismus is present in most albinos. The horizontal perimeter of the cornea was flattened in the six Moon-Children examined.

Laboratory tests showed nothing of importance, but a physiologic defect is suggested because of the high PBI,[20] and the distinctive body odor.

The voice of Moon-Children differs from that of the controls. It is weaker, has a higher pitch and less resonance.

The I.Q. of Moon-Child albinos is not in the mentally retarded range, but they show psychiatric manifestations.

The Moon-Children lead an abnormal life, restrained in many activities by their physical condition. They are largely rejected by the opposite sex. The inability to compete physically often leads them to sedentary and intellectual pursuits. Because of their weakness and rejection they develop anxieties to which they react by overcompensation or regression.

Further data should be collected on the Moon-Children in all of the areas studied. An investigation of dreams and their interpretations, which are so important to primitive peoples, should reveal even more of their psychiatric make-up. The possibility of early retarded physical development should be examined at the time of teething, walking and talking.

Our examination of the Moon-Child Syndrome reveals important alterations in morphology and behavior, which appear as pleiotropic manifestations of the albino gene, much as one finds alterations of morphology, physiology and behavior associated with the presence of certain coat-color genes in mammals.

Résumé

En général on a l'impression que les sujets contrôl Cuna* de peau couleur brune sont des types bien plus masculins dont la musculature est bien plus developpée que celle des enfants lunaires.** Cette impression est sup-

* Tribu indien de Colombie et Panama.
** Type d'albinos trouvé parmi les Cunas.

portée par plusieurs données. Le poids moyen des six mâles ayant fait l'objet des études au Milledgeville State Hospital (Georgia, U.S.A.) est presque 10% au dessous de celui des sujets de peau brune formant les contrôls. Les os des albinos sont plus délicats, ayant le sédiment calcaire moins élevé que celui des bruns.

Les sujets contrôl de peau couleur brune ont des mesures plus élevées en ce qui concerne la circonférence de la poitrine et de la tête, le diemètre pariétal et fronto-occipital de la tête, la longueur du visage, la longueur mandibulaire, la longueur nasale, la longueur et distance intra-orbitales, la longueur du fémur plus longueur de tibia, la longueur de tibia, la longueur de pied, la circonférence de carpe, la longueur du radius et la longueur de l'humerus plus longueur du radius, mais les proportions des enfants lunaires n'excèdent pas les limites normales en général.

D'un autre côté, la longueur du nez est plus grande proportionellement que celle des sujets contrôl. L'enfant lunaire a la tendance d'être brachycéphal, et la pente de son front est plus graduelle. Les os de la tête dans la région nasale semblent être sous-développés, et les dents poussent moins en avant. La pointe de la machoire des albinos a la tendance d'être plus aiguë.

Les oreilles des albinos sont plus proéminentes que celles des sujets normaux. Le cartilage auriculaire supérieur est hypertrophié, devient dur, et des nodules se forment le long de la limite périphérale du pavillon de l'oreille. Le cartilage nasal s'allonge et c'est possible qu'il existe l'hypertrophie des cartilages de la gorge.

Les cheveux sont plus fins que ceux des sujets contrôl. Dans l'enfance on peut observer des fois des cheveux aux côtés des joues, et il y en a toujours sur les parties distales des membres. Avec l'age, la couleur des cheveux peut changer du blanc en passant par le jaune jusqu'au brun et même châtain. De très grandes tâches de rousseur et des brûlures causées par le soleil developpent sur la peau. L'exposition continue au soleil tropical cause l'hypertrophie de la peau, sauf en dessous des tâches de rousseur qui, de ce fait, se trouvent à un niveau beaucoup plus bas que la surface hypertrophiée. La peau des rides à l'intérieur du coude dégenère. On peut noter dans la peau hypertrophiée du corps des kératoses séborrhéiques, des elastoses solaires et des petits carcinomas squameux potentielles.

Normalement les yeux des enfants lunaires sont gris-bleus avec des accents bruns aux pupils, mais des fois ils changent en brun en passant par des couleurs variées. Tous sont myopes. Le nystagmus latéral graduellement se developpe chez les albinos à l'age d'un mois environ. Presque tous les albinos souffrent du strabisme. Le périmètre horizontal de la cornée apparaît diminué dans les six enfants lunaires sous étude.

Les tests de laboratoire ne montraient rien d'anormal, mais il est probable qu'il existe un défaut physiologique en vue de leur PBI (iode associé aux protéines) élevé et de leur odeur charactéristique.

La voix des enfant lunaires est d'un ton plus haut, et moins résonnante. Le quotient d'intélligence des albinos n'est pas celui des sujets retardés mentalement, mais ils manifestent des symptomes psychiatriques. Les enfants lunaires mènent une vie anormale car beaucoups d'activités ne leur sont pas possible à cause de leur condition physique. En grande partie ils ne sont pas acceptés par le sexe opposé. Puisqu'ils ne peuvent pas soutenir la concurrence dans le domaine physique, ils sont souvent amenés à des activités sédentaires et intéllectuelles. A cause de leur faiblesse et leur rejet ils developpent des anxiétés auxquelles ils réagissent par compensation exagérée ou par régression.

Il serait intéressant de collecter des données nouvelles sur les enfants lunaires dans les régions qui ont été soumises a cette étude. Une investigation de leurs rèves et des interprétations de celles-ci—si important aux peuples primitifs—pourra reveler d'avantage leur état psychiatrique. On devrait étudier la possibilité d'un retardement physique précoce à l'age de la dentition et quand les enfants commencent à marcher et à parler.

Notre examin du syndrome de l'enfant lunaire nous montre des changements importants du point de vue morphologique et de comportement qui semblent être des manifestations pléiotropiques du gène d'albinisme, de la même manière qu'on trouve chez les mammifères des altérations de morphologie, physiologie et de conduite associées avec la présence de certain changes de couleur de couverture extérieure.

Resumen

La impresión general es la de que los sujetos testigos de la raza india Cuna (Colombia, Panamá), de piel oscura, tienen características más masculinas y que su musculatura se halla mejor desarrollada que en los albinos. Esta impresión tiene sus orígenes de diversas observaciones. El peso promedio de los seis niños lunares (tipo de albinos) estudiados en el *Milledgeville State Hospital* (Georgia, E.E.U.U.A.) fue casi un diez por ciento inferior al de sujetos de piel oscura. Los huesos de los albinos son más gráciles y contienen menos depósitos de calcio que los de los testigos de piel oscura.

En los testigos de piel oscura, el perímetro craneano y torácico, los diámetros parietal y fronto-occipital, el largo de la cara, mandíbula y nariz, el tamaño de las orbitas y la distancia interorbitaria, el largo del fémur más el largo de la tibia, el largo de la tibia, pie y radio, el largo del húmero más el del radio, y el perímetro de la muneca, son mayores que en los albinos. En los sujetos albinos, sin embargo, las proporciones se conservan, por lo general, relativamente normales.

El largo de la nariz de los albinos es proporcionalmente mayor que en los sujetos testigos. El niño lunar tiende a ser braquicefálico; además, la frente es de inclinación más gradual. Los huesos craneanos que participan en la formación de la región nasal parecen subdesarrollados. Los dientes son menos procidentes. La barbilla es más afilada en los albinos.

Las orejas de los albinos son más separadas del cráneo que en los sujetos normales. El hélix se hipertrofia y endurece y se forman nódulos en el borde del pabellón. Los cartílagos de la nariz se alargan y tal vez se produce hipertrofia de los cartílagos laríngeos.

El pelo de los albinos es más fino que en los sujetos testigos. En la niñez, es posible encontrar vello a ambos lados de la cara y siempre en la región distal de los miembros. El pelo puede cambiar de color con la edad, desde el blanco al amarillo y pardo y hasta el pardo-rojizo. En la piel se producen grandes pecas y quemaduras por el sol. La exposición continua al sol tropical causa hipertrofia cutánea, excepto debajo de las pecas que quedan deprimidas en la superficie de la zona de piel hipertrofiada. Se produce atrofia en el pliegue de flexión del codo. En las zonas hipertrofiadas de la piel se observan regiones queratósicas seborreicas, elastosis solar y pequeños carcinomas escamocelulares potenciales.

El iris de los niños lunares es corrientemente azul-grisáceo con areas pardas alrededor de la pupila. El color claro puede a veces virar a diferentes tonos hasta el pardo. Estos niños son miopes. En los albinos, a la edad de más o menos un mes, se produce nistagmus lateral, primero lento y luego más rápido. La mayoría de los albinos presenta estrabismo. En los seis niños lunares examinados, la córnea se hallaba aplanada.

Los exámenes de laboratorio no revelaron nada de importancia; sin embargo, parece existir algún defecto fisiológico por cuanto la yodoproteína sanguínea se halla elevada. También presentan un olor corporal característico.

La voz de los niños lunares difiere de la de los testigos; es más débil, de tono más agudo y de menor resonancia.

El cuociente de inteligencia ("IQ") de los niños lunares no queda dentro de los límites del retardo mental; sin embargo, presentan manifestaciones psiquiátricas.

Los niños lunares no viven una vida normal; muchas de sus actividades se restringen a causa de sus condiciones físicas. Con gran frecuencia son rechazados por el sexo opuesto. Su incapacidad para competir físicamente a menudo los lleva a una vida sedentaria y a desplegar actividades intelectuales. A causa de su débil constitución y al aislamiento de que son víctimas, sufren angustia a la que reaccionan con compensaciones exageradas o regresión.

Es necesario acumular más información sobre los niños lunares en todas las fases de su estudio. Una investigación de los sueños y su interpretación, de tanta importancia en sujetos primitivos, puede revelar mayores datos sobre sus rasgos psiquiátricos. La posibilidad de retardo temprano del desarrollo físico puede verificarse estudiando estos sujetos por ocasión de la dentición, la marcha y el lenguaje.

Nuestro estudio del síndrome del niño lunar ha revelado la existencia de importantes alteraciones morfológicas y de comportamiento que se traducen por manifestaciones pleyotrópicas del gene albino, muy semejantes a las alteraciones morfológicas, fisiológicas y del comportamiento que se asocian con la existencia de ciertos cambios en el tegumento coloreado de mamíferos.

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Cuna Moon-Child Albinism

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In 1941, black (non-agouti), hooded (piebald) and albino variations of the rat were observed to be external indicators of unsuspected modifications in glands, sense organs and brain resulting in unique syndromes of body size, morphology, physiology and behavior trend,[1] called "marks of domestication" by Darwin.[2] These modifications tend to produce tame behavior, and their effects are additive in that if black, hooded and albino variations cropping out in a wild gray stock are combined in a single individual, this homozygous animal with triple recessive traits will resemble tame laboratory albino rats in its quiet and typically docile reactions.[3]

These "marks of domestication" in rats are not caused by mutant genes linked in the same chromosomes with the coat color genes, as some have supposed, but rather are due to pleiotropic manifestations of the pigment-modifying genes themselves.[4-6]

The same phenomena were observed in a 12-year study of ranch bred mink, pigment gene pleiotropy being responsible for body size[7] and proportion[8] variations, as well as exceptionally tame behavior,[9] when certain coat color genes were combined, as in the case of the Norway rat.

When the concept of pigment gene pleiotropy is extended to a mammal with a higher level

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7. Keeler, C., *Bull. Georgia Acad. Sci.*, 19: 22-60,1961.
8. Keeler, C., & Moore, L., *Bull. Georgia Acad. Sci.*, 18:69-84,1960.
9. Keeler, C., & Moore, L., *Bull. Georgia Acad. Sci.*, 19:66-74,1961.

of cerebration, the Red fox, the amber coat color variation (a homozygous combination of chocolate, blue, and black mutations) is observed to be accompanied by small adrenal glands[10] and reduced nasal development. This exceptionally tame animal contrasts strongly with the wild, fear-torn Red fox that is constantly running away from situations in his environment. Thus, the phenomenon appears to be universal and might be expected to apply to such pigment variations in man as albinism and red hair.

Data collected on 14 expeditions to San Blas, as well as from extensive laboratory examinations of six Moon-Child boys and six dark-skinned controls,[11] permits description of the Moon-Child condition as a syndrome.*

Incidence

The incidence of Moon-Child albinism among the Cunas[12] is about 45 times as great as that for albinism in the United States and it will probably increase, since light colored heterozygotes tend to intermarry, and albino infanticide decreases with the introduction of Christianity and Western culture.

Anthropometrics

Laboratory measurements[11] were taken of weight, height, chest circumference (inhale and exhale), wrist circumference, length of tibia, length of femur plus tibia, metacarpal dimensions, head circumference, parietal diameter of head, fronto-occipital diameter of head, facial length, nasal length and manometer deflections. Overall size of the albino body is less than that of the controls. The albino face tends to be flattened, as seen in profile photographs[13] confirmed by x-ray studies[14] and direct observation. Similar profile changes accompany certain coat color mutations in rats.[15]

Fingerprints of Moon-Children do not differ significantly from those of dark-skinned controls.[13]

Skeleton

Cuna albinos tend toward brachycephaly and their bones are gracile, those of the fingers revealing less calcium[11] deposition than those of controls. X-rays taken in the Walter position show a narrower nasal

*The 146 Moon-Children in San Blas Province, Panama, are so called because their condition is thought by the Cunas to be caused by the father or mother looking at the moon during gestation. There appears to be no doubt that a Cuna Moon-Child is a true generalized albino appearing on an inbred tribal background tending toward a uniformity in expression not to be found in heterogeneous populations such as exist in the United States.

10. Keeler, C., *Mind Over Matter*, 9:16-30,1964.
11. Keeler, C., *Derm. Trop.*, 3:1-11,1964.
12. Keeler, C., *J. Heredity*, 54:115-120,1964.
13. Keeler, C., Unpublished.
14. Keeler, C., *Mind Over Matter*, 9:30-41,1964.
15. Keeler, C., *J. Tennessee Acad. Sci.*, 28:49-53,1953.

region and the malar eminences to be farther in from the lateral periphery of the skull. The Moon-Child forehead slopes more gradually. The teeth protrude less, the mouth tends to be wide, and the chin bones tend to be more pointed.

The tissue under the chin of the albino is pendulous, the lips hypertrophied and the nares enlarged.

The nose is elongated, the ears flare and cup and nodularities develop along the brim of the superior auricular cartilage. The throat cartilages are somewhat hypertrophied, the vocal cords in two out of six being impossible to visualize with a speculum. Chest shapes of Moon-Children are usually abnormal. Arthritic ankyloses of the finger joints are common.

Skin and Hair

Head hair of albinos is invariably finer than that of controls. Lanugo-like hair may be found at the sides of the face and on the ears in childhood and is almost universally present on the distal segments of arms and limbs in childhood and youth. On the lower arms, this hair often disappears in later life when the skin becomes hypertrophied.

Sweat pores are sometimes either destroyed or occluded on heavily hypertrophied areas, since sweating ceases.

Pigment of the light blue iris and of the hair may darken, the latter changing from white to yellow and, in some cases, to red and even brown. The skin of the young Moon-Child is pink, softened by short, white hair all over the body. The skin appears to be extremely thin because the capillaries are often evident.

With exposure to tropical sunlight, enormous freckle-blotches appear and boys of 10 frequently exhibit a number of infected sunburn lesions at the same time. Later, the skin hypertrophies around the pigmented blotches, leaving them sunken below the general surface of the skin. Degenerate furrows often occur inside the elbow joint. The hypertrophied skin exhibits seborrheic keratoses, solar elastosis and small potential squamous cell carcinomas (Figure 1). With increasing age, there is a gradual increase in the number and severity of lesions and, in 1965, of 40 albinos examined, 11 showed cancerous areas, nearly all being squamous cell carcinomas that metastasize and constitute the principal cause of death in those Moon-Children who live to adulthood (Figure 2). Statistics show that Moon-Child girls live longer than their male counterparts, probably because they are more

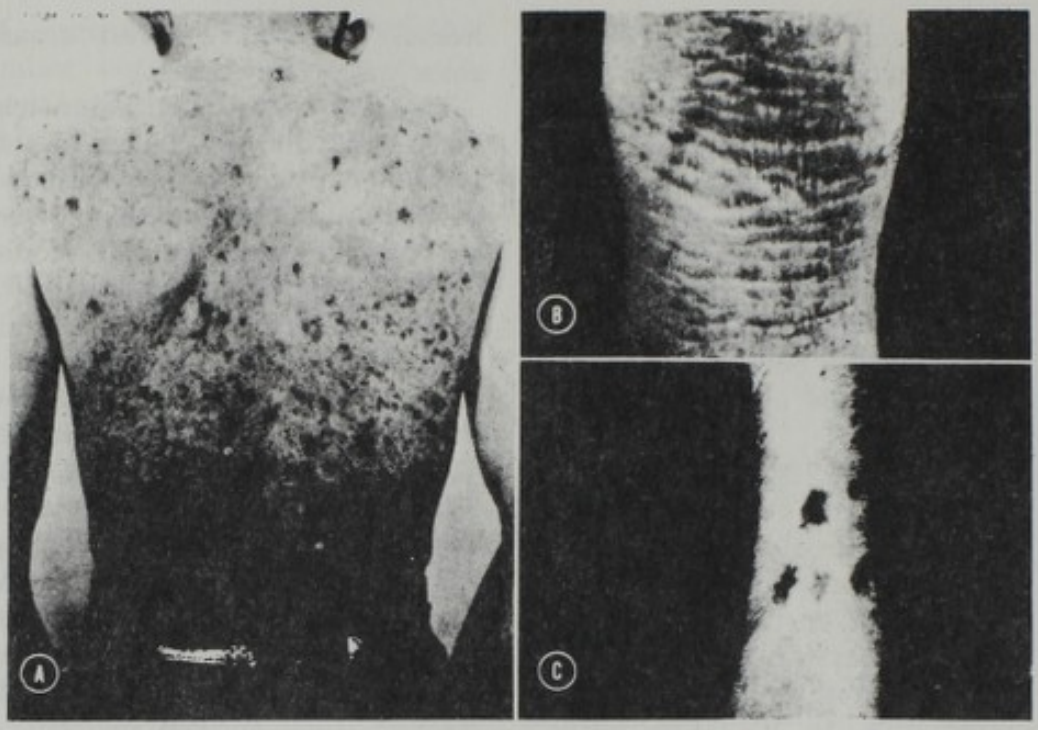


FIGURE 1

Moon-Child characteristics. A, back showing actinic keratoses, seborrheic keratoses, freckles, solar elastoses, infections. B, degenerative creases opposite the elbow. C, freckle blotches and hair on the lower arm. (Normal Cunas lack this hair.)

likely to be protected.

Teeth and Eyes

The teeth of Moon-Children do not appear to show more defects or less calcification than their controls. Many are mouth breathers.

The fundi of the eyes[16] of six Moon-Children were typically albino with coroidal vessels visible. Patches of sclera showed between the vessels and the macular region was abnormally reddened. The optic disc was visualized in all Cunas. There is usually a slight defect in their color vision.[13]

Lateral nystagmus of the fixation type appears at one month of age. Of the several hundred Moon-Children seen during 16 years, only one appeared not to be myopic. Corneal astigmatism was found in all six Moon-Children examined in the clinic, and

16. Courtney, R., & Keeler, C., *Am. J. Optom.*, 41:283-292,1964.



FIGURE 2

Squamous cell carcinomas in Moon-Children. *Left*, recurrence at site of old operation. *Right*, large carcinoma on cheek. This woman died six months later from internal metastases.

corneal curvature was flattened along the horizontal perimeter in five, with the flattened band tilted low laterally and high medially in the sixth. Strabismus is present in all Moon-Children, and in adults the external lateral muscles cease to function.

The tonal quality of the Moon-Child vocal and speaking voice, especially in males, was lighter and of a higher pitch than that of controls. Ultraviolet spectrum analysis[11] of urine suggested that male sex hormones of Moon-Children are deficient.

Laboratory Tests

Three pairs of Moon-Child males and controls were tested for complete blood count, sedimentation rate, sickle cell prep., thymol turbidity, cephalin flocculation, total cholesterol, potassium, sodium, uric H+, glucose, urea nitrogen, protein-bound iodine, urinalysis, and for stool ova and parasites. Nothing significant was found except that, surprisingly enough, the albinos

had elevated protein-bound iodines, two of them within the range of thyrotoxicosis. They had a low specific gravity.

Special tests included hemoglobin, serum electrophoresis, urinary acid secretion, Mosenthal's urinary concentration and typing for blood groups, antigens A,B,O,D,E,C, c,e,Cu,[8] F,M,N,S, K, G, Le^a, Le^b, Fy and Di^a. All Cunas tested were O+. One control was Diego-positive. One albino excreted β amino-isobutyric acid in large amounts.

Among 12 Indians examined, five had slight to pronounced cardiac hypertrophy due to unknown causes. The QRS ventricular pattern of the S1 S2 S3 type was found in four out of five controls, and once in six albinos. There was a tendency to left axis deviation in albinos and to right axis deviations in controls. In albinos, the horizontal position tended to predominate; in the controls, the vertical electrical position predominated.

General Health

The general health of Moon-Children appears to be poorer than that of the controls. As children, they carry infections of nose and throat. Their mosquito bites become infected. After puberty they lack energy, avoid athletics and tend to move slowly as a rule.

Intelligence

Tests with Arthur Adaptation of the International Performance Scale (two and one-half to 12 years), I.P.A.T. free Test of "G," three sub-tests of the Wechsler Adult Intelligence Scale, Draw-A-Person Test, Bender-Gestalt Visual Motor Test and Rorschach, although not completely satisfactory, led to the conclusion that there is little or no difference in basic intelligence between the Cuna albino and the normal dark-skinned control.[17]

A comparison of two albinos with two controls showed a basic difference in their level of emotional development and their use of defense mechanisms. There was a striking masculine identification in the control group. They were more overt in expressing hostility, were openly aggressive and had an active interest in the opposite sex. On the other hand, the albinos revealed a passive, dependent, feminine orientation. They showed little active interest in the opposite sex and tended to relate to its members on a prepubertal psychosexual level. They exhibited greater anxiety and used defense mechanisms to ward off this anxiety. Denial was pronounced. The defense mechanisms were

17. Stewart, H., & Keeler, C., *J. Gen. Psychol.*, 106:319-324,1965.

weak, breaking down quickly under moderate stress and releasing the underlying hostility and aggressiveness or taking the form of withdrawal.

Psychiatric Examinations

Psychiatric examinations (by Spanish-speaking psychiatrists) covered relations between parents, mother and patient, father and patient, siblings and parents, as well as sexual development and functioning, social development, relations to women, adaptational responses and psychosomatic disorders.

Moon-Children, especially males, are restrained in many activities by their physical condition. Four albinos (three in their late twenties) had had no sex experience, whereas the other two (in their middle thirties) had been able to attract girl friends by music or dancing.

Traditionally, Moon-Children were forbidden to marry but, with the pressure of Western ideas flowing in from Panama and the United States, they now assert their "right" to marriage and family. In spite of this, few albino males marry.

Profile body photos in the nude reveal good posture and a normal phallic turgidity in dark-skinned controls, but poor posture and complete flaccidity in albino males. Male homosexuality is quite common in the Cuna tribe. The author has record of four instances of male homosexuality between albino and dark-skinned males on the San Blas coast, the albino playing the female role in each ease.

Conclusions

Heredity may account for a syndrome of skeletal changes (aside from cartilage proliferation), possible macular alterations, flattened corneal curvature, distinctive odor, reduced ability to produce antibodies and glandular imbalance, especially in males. This latter defect apparently accounts for much sexual limitation, physical inactivity, stubbornness and distorted outlook upon the world. Most of the other characteristics in the description of Moon-Child albinism as a syndrome should be looked upon as the result of the tropical environment (especially heat and sunshine) impinging upon the altered genetic constitution. ■

XLVII

Keeler, C.E. Note on odor and sweating of Cuna Albino. Dermatologia Internationalis. In Press.

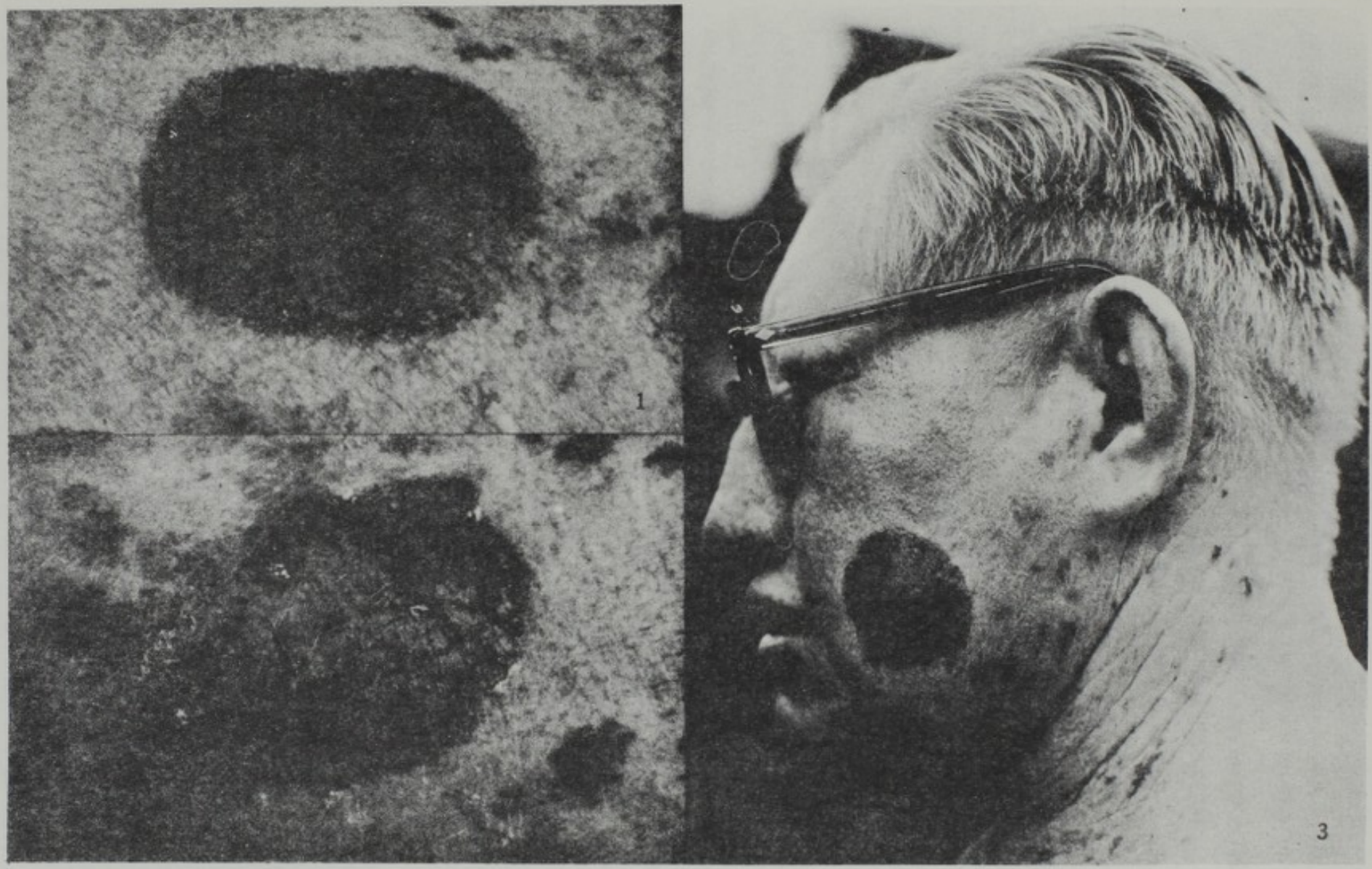
SUMMARY

Previously we had reported on the characteristic odor of Cuna albinos, but that such an odor as we described exists was denied by several leading Dermatologists.

For this reason we sought to collect more data. We felt that on the San Blas Coast lacking the plethora of odors of civilization in a place where there are many albinos, and in a culture where the sense of smell is very important our observations could be put to a rigorous test.

We asked 12 Cuna men, some being medicine men and one being an island Chief. They all agreed that albinos possess a repulsive bodily odor, especially when sweating. Most of them said they smelled like a swamp and that the odor was worse in adults. A high rate of arthritically paralyzed fingers was also noted in the albino Cunas.

We painted iodine on cheek, upper arm and lower arm of a Cuna albino male, aged 42, rubbed cornstarch into his pores and made him sweat. Photos showed great areas in which the sweat pores are occluded. It is estimated that ½ of the sweat pores are not functional on the face, 1/3 on the upper arm and 7/8 on the lower arm.



Occlusion of sweat pores on (1) upper arm, (2) lower arm and (3) cheek of a 42 year old Cuna albino. For procedure, see text. Photos by Robbie Hattaway, Jr.

XLVIII

Keeler, C.E. Note on Olfacto-Genes. J. Hered. In Press.

SUMMARY

Melanin pigment is the end product of a series of complicated chemical reactions involved in phenylalanine-tyrosine metabolism. Recessive hereditary defects breaking this chain produce phenylketonuria, albinism and alcaptonuria. Phyenylketonuria was discovered through its musty smell and alcaptonuria produces a distinctive bodily odor. The presence of the chain amino acids valine, leucine and isolucine in Maple syrup disease is accompanied by the unique scent that confers its name. A criterion in the diagnosis of cystinuria is the characteristic replusive odor of cadaverine and putrescine.

Our data shows that albinism also possesses a distinctive odor, as does phenylketonuria and alcaptonuria.

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XLIX

CUNA MOON-CHILD PHYSIOGNOMY

Clyde Keeler, Milledgeville, Georgia, U. S. A.

Sheldon,[1] following the early work of Kretchmer[2] and others, attempted to correlate specific physical types with behavior. By detailed measurements he classified all general physical types of mankind and all personalities and found correlations between certain physical types and certain personalities. He superimposed his temperamental distribution over his physical distribution in what he termed a Tripolar Psychiatric Orientation. He then sampled certain professional groupings of mankind and found that they tended to aggregate in specific areas of this map of physical and temperamental types.

Although we believe that Sheldon went too far in identifying such things as "criminal types" with specific areas on his Tripolar Psychiatric Orientation, except insofar as criminals tend to be active physically and retarded mentally, a numerical description for classifying all types of mankind both physically and temperamentally should be of scientific value. However, such a classification does not identify any of the myriads of genetic factors in the gene pool that combine in all possible combinations to produce this physical and mental variability.

One of the most important classes of genetic factors involved in producing the variability measured by Sheldon are the genes influencing glandular balance, but he has merely classified mankind as a whole and cannot evaluate the shifts in one direction or another produced by specific genes, for example, those affecting the hormones.

Sir Arthur Keith[3] attempted to account for physical differences between the major human races by postulating different hormonal balances for each race. With this idea he characterized the facial features and bodily forms of the other races compared to Caucasians: thus, for Mongolians: reduced adrenals, reduced interstitials, reduced pituitary, reduced thyroids; for Negroes: greatly reduced adrenals, reduced interstitials, reduced pituitary, reduced thyroids; for long-legged Nilotic Negroes: greatly reduced adrenals, greatly reduced interstitials, reduced pituitary, reduced thyroids; for pygmies: greatly reduced adrenals, reduced interstitials, greatly reduced pituitary, reduced thyroids.

I do not know what significant dissection data or hormonal analyses there may be to support this classification. Crosses between persons typical of the major races of mankind usually produce blends, indicating that the genetic differences are multifactorial.

The question arises as to whether the effects of single genes upon morphology and behavior can be identified within the great spread of human variability, since it is known that abnormal mendelian hormonal variations can produce modifications of face shape and body form, as in the case of achondroplasia.

It was shown previously that within inbred strains of rats the effects of single genes on face shape,[4] and body size[5] could be detected. The effects on bodily proportions[6] and on body size were demonstrated for mink.[7]

> The wild gray Norway male rat has a strongly constructed head with powerful jaws and a well-built nose, for olfaction is a dominant sense in the wild gray Norway rat. The albino mutant has a nose somewhat reduced and shortened. The eyes are not prominent and this may indicate thyroid deficiency, although the albino mutant is a plucky and vicious antagonist. The black (non-agouti) mutant has the face pointed with a receding upper lip and jaw. The olfactory bulbs are greatly reduced in size as is the brain. The eyes are fairly prominent but less so than in the wild gray. One observer remarked, They look as though you stuck their faces into a pencil sharpener! Black mutants do not

From the Research Laboratory, Milledgeville State Hospital, Milledgeville, Georgia, U. S. A. This investigation was supported in part by an NIH Research Grant GM. No. 10472-01 and an NIMH Small Research Grant No. MH 10164-01.

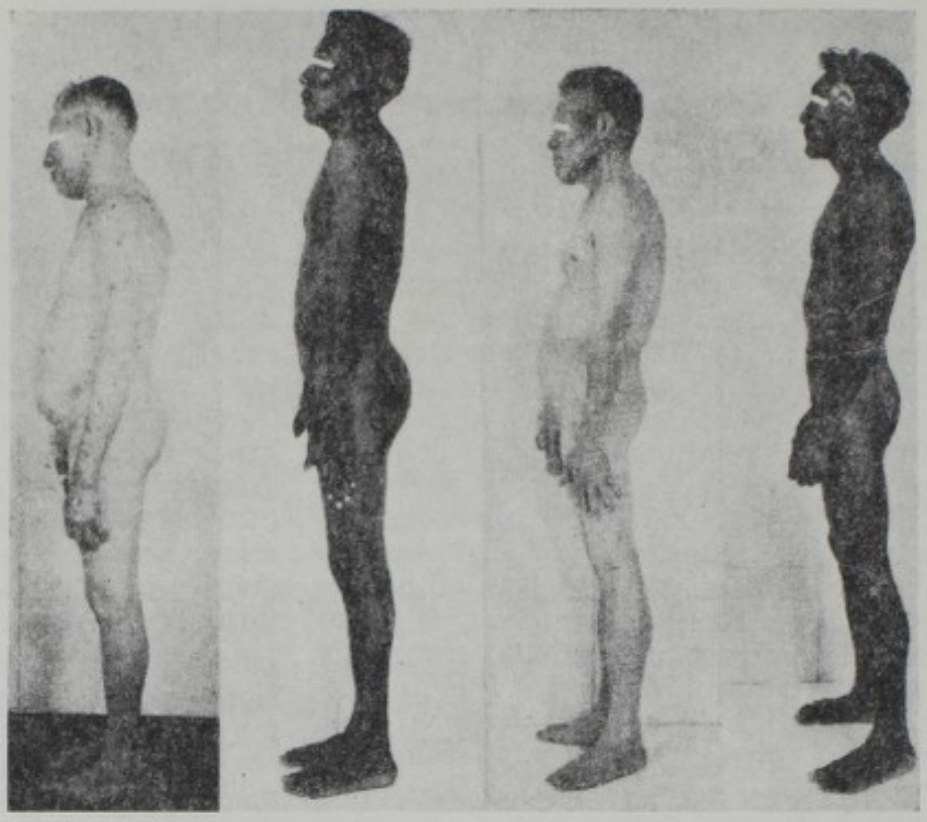


Fig. 1 — Two albino boys in profile compared with their brown-skinned controls paired for age and sex.

compete well with grays in battle. The black-piebalds have long, narrow heads with pointed faces and drooping noses. Their eyes usually protrude. The curly rat is known to have enlarged thyroids, and as a result, its behavior is nervous and erratic. Its face is pointed. The jaws appear weakly developed and the eyes pop. The cinnamons tend to become acromegalics with wide heads, massive lower jaws, and relatively small pop eyes. The upper lip does not appear to be enlarged. Cinnamons tend to grow larger than wild grays and hence the pituitary is probably hyperactive. Such an overactive pituitary would account for the trend toward acromegaly.

Experiment

We have compared six Cuna Indian Moon-child boys with brown-skinned controls paired with the albinos for sex and age. The albinos averaged smaller in size than the brown-skinned controls, and a high percentage were brachycephalic. We have the impression that the malar eminences of the albinos do not protrude, on the average, as much as do those of normal individuals. Our x-rays of the skull, taken in the Walter position, revealed that there is probably a real difference, the six Moon-children having malar eminence lines at a greater distance from the lateral periphery of the skull. Closer inspection showed this to be due to a more narrow width of the nasal region.

In profile there is a more gradual slope to the Moon-child forehead. The teeth

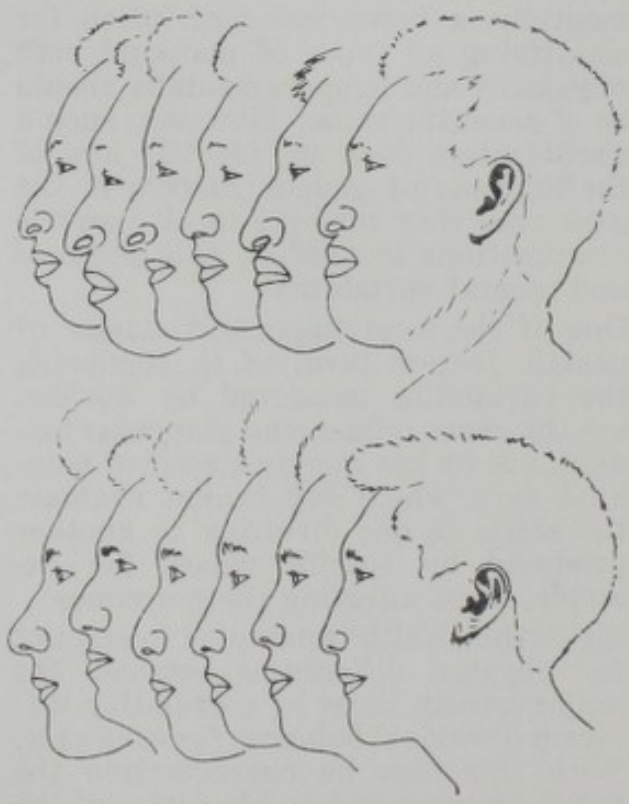


Fig. 2 — Profiles of twelve Cuna Indian males traced from photographs. Above: Moon-child albinos. Below: Normal brown-skinned controls. Albinos and controls are paired for age.

Table I. *Relative Values for the Profile of Lip Area as Measured by the Analytrol.*

	Pair 1	*Pair 2*	*Pair 3*	*Pair 4*	*Pair 5*	*Pair 6*
Albinos	24.1	28.3	25.0	25.4	33.0	29.5
Brown-skinned controls	11.9	12.3	11.9	12.7	14.5	15.0

Albino mean $= 27.5 \pm 4.03$
Control mean $= 13.0 \pm 0.38$
Difference $= 14.5 \quad 4.24$
Significance $= 14.5 \div 4.24 = 3.42$

protrude less, and the point of the jaw tends to be more sharp than in the controls. The ears cup and the nasal cartilage appears to have elongated.

Profile photographs of the six Cuna albinos and their paired controls (Fig. 1), were enlarged for shape comparison so that the distance from the brow ridge to the external auditory meatus was of equal length, after which the facial profile was sketched on a sheet of transparent plastic placed over the photograph. The albino profiles are arranged together as are the profiles of normal brown-skinned boys (Fig. 2).

Four shape differences are at once apparent: (a) the hooking of the albino nose, (b) the large size of the albino nares (c) the large albino lips, and (d) the droop of the albino chin. It is difficult to obtain measurements of these characteristics for comparison. However, we made cut-outs of black paper representing the sizes and shapes of the nares and the lips on the profiles of the size-adjusted photographs of the individuals in the study. These were pasted on electrophoresis strips and evaluated on a Beckman Analytrol (Table I). From these data it is apparent that the profile of the lips of albinos has an area 47.2 per cent larger than that of their controls.

The size of the nasal aperture gave the results shown in Table II. From these values it is apparent that the area of the albino nares is 58.8 per cent larger than that of the controls.

It is difficult to measure accurately the curve or profile area of the nose, and almost impossible to measure the pendulousness of the chin. However, it had been determined previously that "the greater mean length of the albino nose becomes statistically significant when it is expressed as a function of facial length, indicating that the albino nose is, in contrast, proportionally longer than the brown-skinned one."

The question arises as to whether these characteristics of Cuna albino profiles are due to heredity, environment or both? The intense sunshine in the tropics does produce hypertrophies, but how much of this effect may be due to the albino gene and how much to the environment playing upon the phenotype it is impossible to say in view of such data as we recorded in our study of rat profiles, which showed that certain single genes may markedly affect the face shape.

In order to test the possibility that some of the difference between the Moon-child profile and that of the brown-skinned Cuna is due to the albino gene *per se* and not to the effect of the tropical sun acting upon this phenotype, a series of profiles of albinos raised in the temperate zone should be compared with suitable controls.

Discussion

To our knowledge nobody previously has described in detail differences between the facial features of Cuna Moon-child albinos and normal Cuna individuals.

Padre Manuel Puig[10] says: "El sol tropical no sólo les ofende los ojos pero les maltrata mucho el cutis haciendoselo caer a pedazos. Son tímidos, retraídos, ineptos para el trabajo y falta de expresión en el rostro."

We found that five of the six albinos that we took to the United States in 1963 were extroverts and that actually only one was "retraído." We agree as to "faltos de expresión en el rostro" and

Table II. *Relative Values for the Profile of Nares Area as Measured by the Analytrol.*

	Pair 1	*Pair 2*	*Pair 3*	*Pair 4*	*Pair 5*	*Pair 6*
Albinos	12.1	14.0	12.5	9.8	14.0	14.0
Brown-skinned control	6.5	7.8	7.8	9.7	9.4	7.8

Albino mean = 13 90 ± 1.52
Control mean = 8.7 ± 1.08

Difference = 5.73 1.86
Significance = 5.73 1.86 = 3.08

believe that this is due mainly to hypertrophy of the skin.

Count Nordenskiöld[11] comments as follows: "They seem, with their bloodshot, blue-brown eyes, squinting in the sun, their strange white skin, which never sunburns, their milk-white or yellow-white hair, most strange in the midst of the normal Indians."

We are in accord with this description except for the unfortunate statement about "their strange white skin, which never sunburns." Elsewhere we have described our observations singly and in collaboration with Donald Moyer, M.D., upon the Cuna albino skin with its general hypertrophy, as well as senile keratoses, solar elastoses, squamous-cell and basal-cell carcinomas, and blistering reaction to sunshine.[12, 13]

Summary

The Cuna Moon-child profile differs from that of normal brown-skinned controls in (a) curved longer nose, (b) larger lips, (c) larger nares, (d) more pendulous chin. The greater length of the albino nose was shown previously to be significant. The lips and nares have been shown in this study to be significantly larger. The pendulousness of the albino chin defies exact measurement, although it can easily be seen.

Sommaire

Le profil de "l'enfant-Lune Cuna" diffère de celui des cas témoins d'ordinaires peaus brunes en ce qu'il a un nez courbé plus long, de plus grosses lèvres, de plus grandes narines, un menton plus pendant. On a montré précédemment que la plus grande longueur du nez de l'albinos a son importance. On montre dans cette étude que les lèvres plus grosses et les narines plus grandes ont aussi leur importance. Le pendant du menton de l'albino ne peut être mesuré exactement bien qu'il existe puisqu'on le voit à l'oeil nu.

Sumario

El perfil del niño Luna de los Cunas es distinto del niño normal de piel oscura utilizado como control en los siguientes caractéristicas: a) la nariz encurvada es mas larga, b) las ventanillas de la nariz son mayores, c) la barbilla es mas prolongada. Se ha ya mostrado que el mayor tamaño de la nariz del niño albino tiene un significado especial. Lo mismo se ha notado en este estudio con respecto al aumento de tamaño de los labios y de las ventanas de la nariz. La prolongación de la barbilla es dificil de medir pero se puede observar facilmente a la inspección.

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L

INTRODUCTION TO RED HEADS

Psychologists usually classify the common statement that Red Heads are "different" in the same category with "old wives' tales". However, some will say that just because they know that they "look different" they will naturally be sensitive. The question is: "Are they different in behavior, and if so, is there a physiological basis for this difference?".

For many years I have asked mothers of both red heads and children of other complexions: "Which child brings home colds, measles, whooping cough and gives them to the other children"? In a majority of cases she points to the red head.

I wrote to the College of Anaesthesiolgy in New York City and asked if red heads reacted the same as others to anaesthetics. The reply was that they usually require much less anaesthetic than others, that they bleed more freely and that they cyanose more quickly. In fact, they teach the slogan: "Beware of the red head on the operating table". I asked an obstetrician at a large hospital if he noticed any differences? He replied that red headed women more frequently than others become suffocated during the last several weeks of pregnancy and have to be placed under oxygen tents. I asked an army surgeon who said that in his long career he may have operated on several hundred red heads. He said he always used a mild type of anaesthetic on them because they could not stand a strong anaesthetic.

At Camp Lejeune I asked the marines. They had a very definite idea of red head sex behavior. At Fort Jackson I inquired about differences in red headed soldiers, and was told that they sweat more freely than others. I asked the air force officers and was told that sometimes red heads have to be brought down from high altitude camps because their lungs cannot take in sufficient oxygen from the rarified atmosphere. I asked the head of the Base Hospital at Camp Lejeune. He said that red headed soldiers are hypersensitive to arsenical drugs. I wrote to the head of a tuberculosis hospital. He was of the opinion that tuberculosis in red heads was farther advanced upon arrival and progressed more rapidly in red headed patients than in others.

I had known personally several red heads that were hypersensitive to alcohol. One day I was riding along with a mink rancher in Iowa. He said, "Doc, what has all this coat color and behavior in mink got to do with people?"

I started to explain red head sensitivity to anaesthetics when his red headed helper called from the back seat: "You're telling me! A month ago I was operated for appendicitis. They nearly killed me - gave me too much ether!"

I discussed the physiological sensitivities of red heads with a bright, red headed girl student of mine. She affirmed that everything I said applied to her. A month later she died in an Atlanta hospital during a simple appendectomy. Too much anaesthetic!

The "hearsay" I have related cannot be taken as conclusive scientific evidence. However, it is suggestive enough to warrent a through investigation of whether or not red heads are "different".

LI

THE RED HEAD SYNDROME

Introduction

Evidence showing that certain mutant hair colors are accompanied by correlated changes in morphology, physiology and behavior tendency have been published for many animals, but particularly for rats, mink, and foxes. It has been demonstrated further that the pleiotropic manifestations of certain coat color genes may be added together in single individuals among rats and foxes to produce more extreme changes in their behavior tendencies. Most profound are the adrenal medulla size variations associated with the coat color genes involved in the experimental behavior syntheses described.

Gross alterations in behavior pattern inherited as unit-characters are well known in mice, pigeons and guineapigs. The literature of medicine is full of simply inherited syndromes that alter the behavior pattern such as Huntington's Chorea, Oppenheim's disease, Friedreich's ataxia, spastic paralysis, progressive muscular atrophy, Thomsen's disease, syringomyelia, paroxysmal paralysis, Leber's disease, von Recklinghausen's and many others.

Pleiotropic effects on behavior associated with hair color in animals are demonstrated by the shuddering of certain pink eye mice when picked up by the tail, or the epileptoid fits of Vienna white rabbits when excited. However, these are to be considered as abnormalities of behavior.

There are two classical examples of mental retardation associated with simply inherited hair color variations. Kline and Sanders showed phenylketonurics to have lesions in the lentiform nucleus, subthalmic nucleus, substancia nigra, red nucleus and dentate nucleus that account for their retarded condition. Phenylketonurics, as is well known, usually have faded hair. The albinistic Chediak-Higashi syndrome not only appears to bring a degree of retardation but contains in premyelocytes and myelocytes peroxidase-positive inclusion bodies. Similar inclusion bodies are found in albino cattle and Aleutian (dilute color) mink, that also exhibit tissue weakness.

In applying these principles to man a number of alterations were found to be pleiotropic manifestations of generalized albinism. For example, profile change, reduced calcium deposit in bones, smaller body size, reduced energy, equatorial flattening of the eyeball, nystagmus, reduced capacity to produce antibodies, reduced sex drive in males with raised pitch of voice, hypersensitivity to alcohol and unique bodily odor are among the diverse alterations associated with generalized albinism among the Cuna Indians.

The present paper will report an attempt to extend observations of pleiotropy to the presence of red hair in man, with special reference to alterations in personality and behavior tendency.

At the outset, it must be admitted that generalized albinism is a syndrome much easier than red hair to identify. Persistent white lanugo, pink skin and nystagmus are usually sufficient criteria for the identification of albinism, but red hair may vary greatly from auburn through bright red and sandy to reddish-tinged blond.

Light sandy will be confused with blonds of particular grades. It appears that the red hair confusion of classification is due to modifying effects of other coat color genes and possibly because there may be several different red variations genetically (phaenocopies) that are indistinguishable to the eye. Albinism in the darker races is accompanied by reddish hair not to be confused with ordinary red hair. Orthodox red hair as a rule behaves recessively to black but dominantly in the presence of a blond gene.

CHEMISTRY OF RED HAIR

Chemically speaking, red human hair contains a red trivalent iron pigment called trichosiderin not found in hair of other colors, suggested as a phenolic iron compound constituting 40 to 60 mg per 100g of hair. It disappears from the hair cortex with the disappearance of certain light brown granules. The implications of different natural hair colors is that somewhere inside such individuals, unique, gene induced chemical reactions are taking place that may, through complicated paths, affect physiological states and through these modify behavioral tendencies. The studies presently to be mentioned suggest psychological and behavior bias for the bearers of red hair.

It was shown by Dutcher and Rothman that red hair contains a greater amount of iron and more ash than hair of any other color. Barnicott found that the highest ranges of trichosiderin are obtained almost exclusively from red hair. However, not only do some red specimens yield a small amount of trichosiderin, but small amounts may also be present in many red-brown and some dark brown specimens. It may be suggested that these latter two types may be heterozygous for a dark allel plus a red allel.

CORRELATIONS OF PHYSICAL TYPE WITH PIGMENTATION

In 1928 Deckner, from a study of 5000 German students, concluded that the cephalic index of brunets decreases much more as the body grows larger than it does in blonds. Blue eyed blonds have the greater height, smaller cephalic index, greater chest circumference, greater lung capacity and greater variability than brunets. In blonds there is a smaller correlation between cephalic index and body size. Although these conclusions tend to show that constitutional tendencies may be associated with pigment variations in man, the study did not include red hair.

RED HAIR AND DISEASE

Beuster, 1937, considered hair and eye color of 500 cancer patients (193 cutaneous, 307 extra cutaneous). He concluded that there were more blond cancer patients than the blond percentage in the general population, skin cancer being more frequent in men, supporting the report of Molesworth and of Epstein for cancer of the throat, oesophagus and upper jaw.

Conitzer 1931 studied red headedness. He stated that two blonds do not have red headed children, and that red hair cropping out from two brunet Jews is darker than red derived from lighter Christians. He confirms the well known fact that usually red heads freckle. He then confuses his story by stating that red hair is most often found in albinos and half albinos. Of course, red hair in Cuna albinos for example, is a different kind of red hair genetically and hence will be omitted from our present discussion. In another 1931 paper Conitzer observed that red hair

is more often associated with blue eyes than with dark eyes. It is my impression that red hair is more frequently associated with blue or green eyes in Massachusetts but with brown eyes in Georgia. This study concluded that "inheritance played a major role in determining familial aggregation of cases but that a Mendelian mechanism could not be established". Penrose found no linkage of red hair with the ABO blood groups and Hauge and Hetwig - Larsen observed no linkage of red hair with blood groups ABO, MN, P, Lewis, Duffy, Kell and Rhesus, observed no sensitivity to P.T.C., eye color and sex.

Bogen states that Hippocratus had indentified red hair to be one of the characteristics of the "habitus phtisicus", meaning pallor, emaciation, poor muscular development and small bones. Bogen studied 144 red haired individuals among 10,000 tuberculosis patients. He concluded that death from tuberculosis in red heads is more frequent than among the controls. Klare and Koester also felt that red hair did not predispose to tuberculosis.

From his study of 150 red haired patients with tuberculosis Hoegen 1952 disagreed, and reported that the course and prognosis of their tuberculosis is "far advanced" in a higher percentage of cases than in non-red heads. This author found that in red heads the disease was relatively unfavorable.

Diehl and Verschuer in their study found 3 pairs of two egg twins. Of these two pairs were red headed. The other pair consisted of a red head and one not red headed. The red headed twin had tuberculosis.

Eli Davis calls attention to the work of Hill and Allen who found 3% of red heads have pneumonia, the same as in the general population. Nor could they find any physical characteristics peculiar to rheumatic fever.

Davis himself observed on the contrary among 100 red haired patients 23 suffering from T.B., 15 with rheumatic fever and 12 with acute tonsillitis. Of 240 patients suffering from rheumatic fever 6% were red haired. Three percent of pneumonia patients had red hair and 7.8% of pulmonary patients had red hair.

Because of the findings of Davis, the subject of rheumatic fever should be examined further.

It has long been known that rheumatic fever runs in families. In 1952 Hill et alii made a genetic analysis of 206 children in 40 families. They must be at least heterozygous for the non-secretor gene.

Since red haired persons are more likely on the average than persons of other hair colors to have rheumatic fever, and since certain persons of the A, B, and AB blood group constitutions known as non-secretors, are more likely to have rheumatic fever, it is suggested that a test of red heads with rheumatism for the non-secretor constitution would be in order.

Because of such physical and physiological correlates in red heads we might well expect deviations in behavior to produce a distinct pattern of response which may be known as the red head personality. The purpose of the present study is to try to indentify this red head personality, if such exists.

There appears to be but one serious study of human red head personality in the literature. This is a doctoral dissertation by Maroske. Forty-five red headed probands were studied psychologically. The greater number of these belonged to the "schizothymic character type and exhibited the typical quality. The correlation between body build and character of Kretchmer applies also to these Red heads".

Previously, we have pointed out the well known tendency of red heads to have thin skins, and possibly as a consequence, a predisposition to allergies of many kinds. They are hypersensitive to anaesthetics and narcotics. They bleed more freely at operations, and cyanose more readily than the average surgical patient. Their lungs tend to be inefficient under conditions of reduced oxygen content, and they sweat excessively in the summertime. Their propensity to long periods of blushing is frequently observed. They are hypersensitive to arsenical drugs. They may be subject to nosebleed, and may be prone to spider markings.

We have approached the rather elusive red head personality problem in several ways: (1) General questionnaire, (2) Skin resistance response, (3) IPAT "The 16 P.F. TEST Form C. (4) Criminality questionnaire.

The general questionnaire suggested differences in psychological and nervous sensitivity, but the skin resistence and IPAT tests did not detect differences from the controls.

CRIMINALITY QUESTIONNAIRE

Most Georgia prison camp wardens had not noticed any differences between the behavior of some red heads as a group and other prisoners. Some had experience with one or two red headed prisoners only. It is probable that many wardens were not observant persons, and some of them seem to answer "no" when they mean "don't know".

One intelligent warden, J.L. Downie by name, was familiar with the problem and had made observations that appear to be quite detailed from which he had derived a definite description of the red head personality:

"The red head seems to be more of an individualist.
He more readily resents authority.
He is more "on the surface".
He wears his emotions on his sleeve."

This warden, who says he has dealt with more than a hundred red headed criminals, feels that the red heads commit more crimes of passion than others, are inclined to be alcoholics and drug addicts, to have tuberculosis and pneumonia more frequently, are more daring than others, become angry and lose their temper more often, violently attack prison enemies more than persons of other hair colors, especially under crowded conditions, more often hold grudges against other prisoners or guards, tend to be bitter and resent prison supervision, are more stubborn and harder to handle than others. He says that he sees these differences but does not know whether they come from heredity or the environment. He feels that they can be trusted just as much as other prisoners, but since the red head is an individualist, he can be trusted best if he receives more individual leeway.

Lt. J.D. Hudgins, 19 years policeman and detective, who says he has dealt with several hundred red headed prisoners tells me: "I always found them to be quick to get mad when first questioned about a crime they had committed. But when they saw you had them and knew what you were doing, they usually broke down and told the truth. Most of them will cry when mad, but after a good cry will come clean, and be honest with you".

Of eight wardens who had noticed that red heads exceed others in at least one item, the results are as follows:

	Yes	NO
Crimes of passion	5	1
Alcoholism	4	3
Drugs	2	3
Daring	6	1
Angry, lose temper	7	1
Be trusted	4	3
Attack violently	5	3
Hold grudges	4	4
Resent supervision	5	3
Stubborn, hard to handle	5	3
	47	25

Von Hentig, Director of the Colorado Crime Survey, found that a far greater percentage of desperados of the Old West were red headed than their assumed percentage in the pioneer population. Assuming that newspaper descriptions of these criminals are correct, one is likely to conclude that von Hentig merely overlooked the fact that the Irish and Scotch Irish were migrating to America in large numbers at the time and that his figures only reflect this fact.

If one looks at the list of red headed desperados described by von Hentig, one finds the names: Harpe, Weightman, Yager, Mike Langan, "Reddy" Sample, Mickey Free, California Joe, Charlie Harper, Wild Bill Cody, Quantrill, Jesse James, Wild Bill Hickok, Sam Brown, Frank James, Bob Younger, Sam Bass and Jack McCall.

Von Hentig makes the interesting observation: "It seems that red-headedness is often combined with accelerated motor enervation".

He turns to the "somewhat higher types of gambler-politicians" where we meet "the mental counterpart" of this "physical acceleration". James Casey,

desperado of San Francisco politics who was finally hanged, received the contemporary description: "His mind was active, his disposition quick and resentful, his temperament nervous-sanguine". Von Hentig says: "On a higher level this easy "ignition" of nervous and mental processes may lead to prominent achievement, if the individuality on which this driving force has been fastened is of superior fiber."To prove his point he cites red headed General Sherman and his red headed aide de camp Lyon. Today, he might have referred to John F. Kennedy.

It is true that most of the names on Von Hentig's roster have an Irish or Scotch Irish ring. But even where red hair was of high incidence among the immigrants, still there was presumbly a much lower percentage of immigrants from Ireland of other hair colors who were desperados.

Earnest Hooten was said to have classified criminals at Sing Sing according to hair and eye color as well as type of crime committed. He was reported to have found the percentage of red heads in the "crimes of passion" class three times as great as their incidence in the prison population at large.

It may be significant that most wardens agree that redheads exceed others in Crimes of Passion, Daring, Becoming Angry and Losing their Temper.

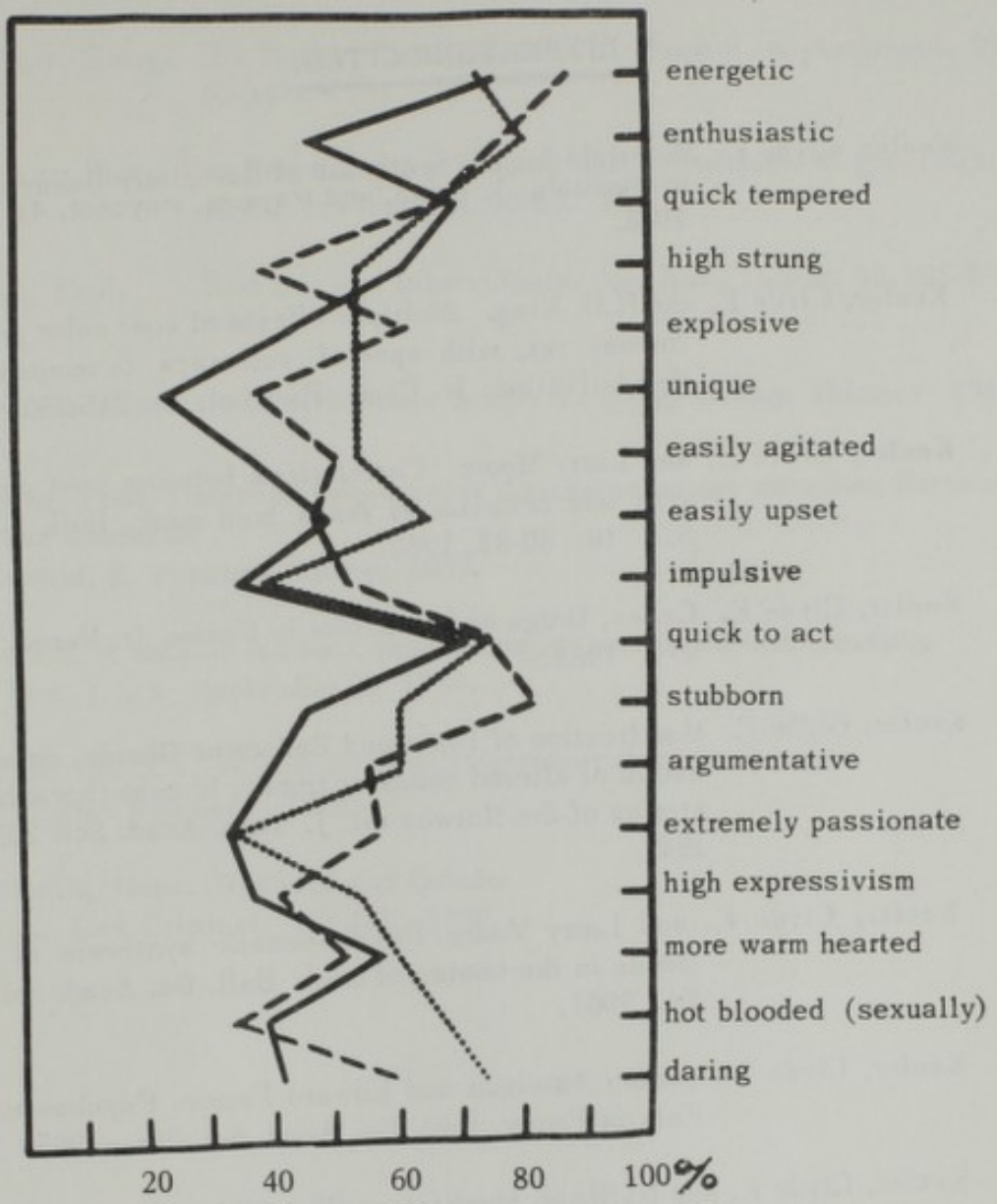
RED HAIR AND SEX.

Eleven service veterans forty years of age or older, having had no red heads in their family to produce prejudice and who said they had been intimate with one or more red headed women, were questioned. Nine of these described the red head personality with warm, friendly, affectionate, very sexual, hot tempered, hot stuff, ready-willing-and- able. Six felt that red heads differed from others in sex activity, seven indicating more intense activity than others, six terming them as "ever ready" rather than as requiring any preliminary stimulation.

OUT STANDING CHARACTERISTICS OF RED HEADS

More than 50% of 118 red heads said that the average red head is energetic, enthusiastic, quick tempered, explosive, easily agitated, implusive, quick to act, stubborn, argumentative, extremely passionate, and more warm hearted. The 48 controls were not aware of all these characteristics, over 50% naming only energetic, quick tempered, high strung, quick to act and more warm hearted. High strung is the only trait mentioned by more than 50% of the controls that more than 50% of the red heads did not admit. This may be a protective answer. Eighty-seven percent of red heads indicate energetic, enthusiastic 77%, quick temper 69%, quick to act 73%, stubborn 81%. It is also noteworthy that a number of red heads felt insulted by the questionnaire refusing to have anything to do with it, and others who filled it out not signing it or permitting their initials to be placed upon it.

Mothers of 15 red heads in addition to children of other pigmentations were asked to check a similar list omitting the item hot blooded. More than 50% checked all the characteristics save implusive and extremely passionate. The description by mothers of red heads emphasizes highstrung, unique, easily upset and daring.



48 controls
118 Red Heads
15 Mothers of Red Heads and Others

CONCLUSIONS

It would appear that red heads possess distinct physiological tendencies and nervous sensitivities. When taken into custody for crimes they tend to exhibit unique hehavior. Red headed females may be more sexual than the average.

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COMMENTS

Robert M. Yerkes: "In this day of stirring events your news about the genetic behavior of personality traits is, for me, the most exciting of all. I scarcely dare believe it, but I earnestly hope that you are right. In that event, and assuming that your conclusions apply to man, you are pointing a way to the modification of human nature, whose chief shortcomings at present are, many of us suspect, temperamental".

Karl S. Lashley: "Your hypothesis concerning the genetics of wildness interests me greatly. Many years ago I noted that in litters containing albino and hooded young there is a marked difference in the reactions of the animals to high pitched sounds, when 18 to 30 days of age. The albinos would come to the front of the cage, the hooded retreat to the back with marked fear reactions".

"It seems to me that you have one of the most important discoveries for psychology that has turned up in a decade and I hope you will carry the studies further".

Abraham Myerson: "Your work which is so dramatic and fundamental, does not in the least astonish me. I have been a strong believer for a long time, and so stated, that temperament and personality are as related to the germplasm as anything else, and that differences in personality were organically or physiologically based".

Theodosius Dobzhansky: "I believe that your approach to the problem is absolutely right. If a mutation taking place in a genetically uniform strain produces multiple effects, this is evidence that these effects are due to a single gene. If we could observe the same mutation to arise in the same strain repeatedly and find that every time it produces the same complex of effects, the evidence would be conclusive".

Edwin G. Conklin: "I want to tell you that I really think you have made a great discovery and that your paper is splendid. - Darwin, long ago, called attention to the fact that albino cats with pink eyes generally had defected teeth and bad temper. I think you will find this in the "Origin" but your work is the most detailed and important of any that I have seen in this field and I am delighted with it."

Earnest A. Hooten: "Just read it and it's swell".

Calvin S. Hall: "This is a dramatic finding. The popular theory of domestication asserts that tame strains of animals came into existence as consequence of the accummulation of a host of gene mutations, each mutation contributing an almost imperceptible amount to the final result of the domesticated strain. According to Keeler and King, a single mutation transforms a wild form into a domesticated one. A major evolutionary step is mediated by a minor gene change."

Barbara S. Burks: "Having now read over your account of data quite carefully, I am as impressed as I was after the first reading. --If the strains are really quite homogeneous for the traits of temperament which you describe, that would really mean, would it not, that "syndromes" of temperament, ie. broad trends of behavior, could be accounted for by single genes?–"A spokesman" has said (there must here be a nameless spokesman) that the paper was a high runner-up for the annual A.A.A.S. prize".

M.F. Ashley Montagu: "The approach of such people as yourself, Allee, Scott, and Jennings to these problems will do more for the founding of a genuine science of sociology than all the wordy treatises of the old-school sociologists put together."

F. Salomonsen, University, Copenhagen: "The pleiotropic effects of the genes affecting coat colour in mammals may also explain the geographical variation in the ratio of the colour phases in polymorphic species. The results of the work in the laboratory bear out the experiences based on studies in the nature".

K. Becker, Robert Koch Institut, Berlin: "it must appear surprising that actually no more than, on the average, 1.8% of all migratory rats in Berlin are black. For this reason one may easily be led to the conclusion of ascribing to the homozygous animal a diminished value of selection. Actually, Keeler could show in laboratory tests that black migratory rats possess a considerably more expressed degree of tameness compared to the wild colored individuals. We believe that this conclusion is confirmed by black rats caught in the wild and then held in captivity, insofar as such animals showed themselves less "unruly" than brown migratory rats deprived of freedom ordinarily do".

M. Jucci, University of Pavia,: "I followed Dr. Keeler's presentation with great interest and immense pleasure. Dr. Keeler's work in this field of research is indeed of extreme importance also on account of its practical applications. At the same time it also carries seeds of great theoretical interest and consequence: firstly, because it clearly demonstrates the influence of the endocrine organs on the racial characteristics concerned with behavior, as in the case of Stockard's dogs: secondly, because it focuses sharply on that interesting pleiotropy of the genetic mutations which combines alterations of both morphology and physiology. It is, nevertheless, interesting to stress that in Nature the physiological rather than the morphological aspects do determine the natural selection and in different degrees force the way for the establishment of a mutant gene in the population. This we should always bear in mind in our endeavor and when we try to move from the genetic field into that of the reconstruction of the process of micro-evolution."

Robert C. Cook ___: This appears to be a capital discovery in advancing our knowledge of intellect and emotions. It has enormously important aspects in the handling of laboratory animals and in the domestication of livestock. Its theoretical implications on the genetics of human mental and emotional differences are only to be guessed.

POSTSCRIPT

We have shown that a number of simple Mendelian gene mutations affecting hair color are accompanied by pleiotropic modifications, physical, physiological and behavioristic. We have demonstrated that by employing the coat colors as external indicators of the syndrome complex within we can add together certain coat color gene mutations to synthesize greater and greater deviations from standard behavior tendencies although this behavior remains within the range of well balanced responses. By this method we have been able to tame rats and to demonstrate tame behavior synthesis in colorphase foxes. The principles should apply to all mammals.

In applying this work to man we have been able to demonstrate pigment gene pleiotropy in albinos and redheads.

Future research in this field must have at its disposal the more refined techniques of biochemistry and the electron microscope. More precise personality and behavior tests must be devised for both man and other mammals. A multidisciplinary approach should be employed. In this future research alterations in glandular balance will be of great importance.

The body fluids such as blood, urine, sweat and others must be analysed for slight pleiotropic variations associated with pigment mutations.

The unique body odor of albinos will be investigated in seeking a therapy for the sensitive, albino skin.

The sensitivities of albino and redheads to anaethetics, narcotics and drugs in general, when thoroughly explored, will lead to prescribing reduced dosages or the rejection of some medications for persons having these pigment variations.

Because of special sensitivity to anaesthetics and narcotics, it is suggested that a fruitful field for future inquiry would be "The relationship of albinism and erythrotricosis to alcoholism and drug addiction".

