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Scope and Method of Study: In this report, the writer has attempted to compile some pertenant data concerning the factors that influence sex determination. The materials used were textbooks and periodicals on Genetics and Cytogenetics. Special emphasis has been given to T. H. Morgan's work on Drosophila melangaster in order to illustrate the relationship between sex chromosomes and sex linkage. It is hoped that the report will answer some of the basic questions envolving sex determination that are normally asked by high school students.

Findings and Conclusions: The sources used in this report clearly indicate that many of the earlier concepts of sex determination are without scientific framework. The determination of sex is not controlled by any single factor. Instead, it is influenced by the chromosomal makeup of the gametes, by endocrine gland secretions and by the environment in which the organism develops. It should be remembered that even though an organism begins to develop as one particular sex, there are certain factors that may cause it to develop in the direction of the opposite sex. Many of the older superstitions concerning this phenomenon have been disproved and more knowledge is being acquired concerning this topic.

ADVISER'S APPROVAL ______________________________

A BRIEF ANALYSIS OF SEX DETERMINATION

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PREFACE

For a number of years the writer has had a sincere interest in the science of genetics, and to a greater extent, the section which deals with sex determination. He was thus eventually inspired to undertake the problem of sex determination as a major topic for his graduate report. The primary objectives of this report are to present a brief and simple introduction to the question of sex determination; to bring together a variety of facts and beliefs gathered from the fields of genetics, cytology and embryology; and to organize the secured material in such a manner that it would give a general picture of sex determination. It should be remembered that the writer is not attempting to give a detailed account of this phenomenom, but is primarily interested in presenting the facts on a level that would be appropriate for high school students. Therefore, many of the complex principles concerning this topic have been omitted.

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CHAPTER I

INTRODUCTION

There are several problems in the Science of Genetics which have excited man's curiosity for many centuries. One of the outstanding questions is: Why are some individuals born males and others females? Scholars, students and laymen have always wanted to know what determines which of these paths a developing young should take and at what point during its development is this important decision made. The best appropriate answer available at present is that sex determination depends mainly upon the type of genetic material contained in the fertilized egg. Half of this material is maternal and the other half is paternal. The role that each portion plays in sex determination will be discussed in this report. There are other factors that exert an influence on sex determination and will also be discussed later. Recent investigations have shown that sex determination is influenced by environmental factors and endocrine gland secretions. However, the influence of these factors is secondary. Many of the early ideas and theory of sex determination were found to be unscientific, and as a result, have been considered obsolete and meaningless. In this report the writer will briefly mention some of the early theories, but the emphasis will be placed on recent concepts of sex determination.

CHAPTER II

CHROMOSOMAL EFFECTS ON SEX DETERMINATION

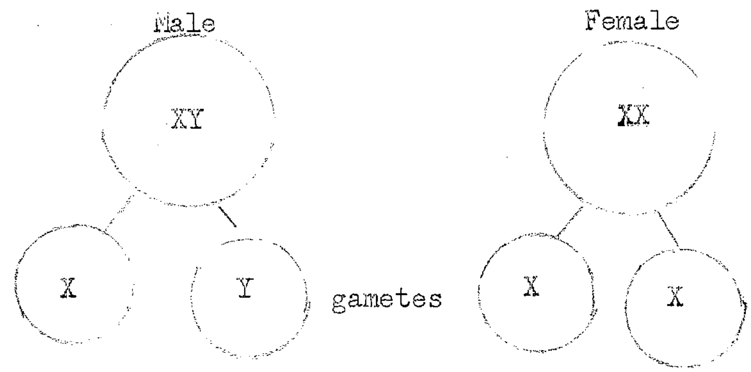
A. Early Theories

There was little progress made in the area of sex determination until man achieved a knowledge of the role of the sex chromosomes. There arose many speculations and unsound beliefs as to how this fate was accomplished. There were three early hypotheses that attempted to explain why some babies were born boys and others girls. Two of these hypotheses were tested. One stated that because a male possessed two testes, the semen from the dexter (right testis) produced a male and the sinister (left testis) produced a female. This belief was common among the Ancient Hebrews and was tested by tieing off or removing one testis from male cattle before copulation. The second hypothesis stated that the sex of the offspring depended upon whether the male or female parent was more heavily sexed. An effeminate male was supposedly capable of producing only daughters. This hypothesis could not be tested. The third and most fantastic hypothesis stated that sex was determined by the direction in which the wind was blowing at the time of copulation. The North wind was said to produce males and the South wind females. Some shepherds tried to produce more females by putting the rams with the ewes only when the South wind was blowing. This hypothesis gained much fame and popularity between the third century B. C. and as late as the seventeenth century A. D. It was respected and accepted by such men as: Aristotle, St. Thomas Aquinas, Pliny and Volateranus. (Dunn, 1951).

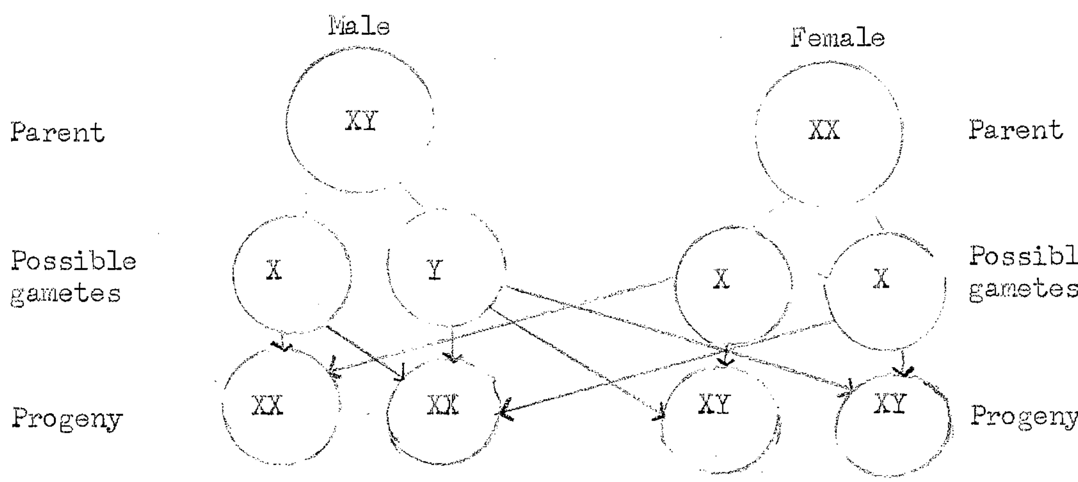
B. The XY Method

A very rare occurrence was observed by Morgan as he studied the inheritance of red and white eyes in Drosophila melanogaster, commonly known as vinegar flies. It was known that red eye color was dominant over white eye color and that a cross between these two would produce all red eyes in the F_1 generation. However, he noticed that the F_2 generation which resulted from a cross between two red eyed flies would produce white eyed males but no white eyed females. This gave Morgan the idea that there was an additional factor involved and that it, in some manner, linked eye color to the sex of the flies.

The results of a microscopic examination of the chromosomes of a male vinegar fly showed that there was an odd one present. It seemed to be hooked-shaped and did not match with its partner. However, no such odd hooked-shaped chromosome was found in females. All the female chromosomes blended with their partners. The gene for white eyes in males was found on the chromosome without the hook. There was no gene for white eyes associated with the hooked chromosome. This was contrary to the Mendelian theory of heredity which stated that each trait was produced by two genes, one located on each member of a pair of homologous chromosomes. These chromosomes were given specific names; the hooked was called the Y chromosome and its straight partner was the X chromosome. This was further evidence to support the fact that males possessed an XY chromosome arrangement and females an XX arrangement. The females produced gametes that were all alike but males produced gametes that were different. The diagram on page four portrays this situation.



The arrangement of sex chromosomes in vinegar flies can be associated with the differences between human males and females. It can be assumed that if tissue from any part of the human body is studied microscopically, it would reveal the XY chromosome make-up for males and the XX for females. According to this situation, it is possible for an individual to have two X chromosomes but never to have two Y chromosomes. The diagram below illustrates this point. (Fast, 1964).



Further studies on Drosophila have shown that the fly posses eight chromosomes in its somatic cells. There are three pairs of autosomes and one pair of sex chromosomes. The results of gametogenesis are similar to the condition found in vinegar flies. The genome of the egg always contains an X chromosome plus the autosomes, but the genomones of half of the sperms contained an X chromosome plus the autosome and half contained a Y chromosome and autosomes. If an egg is fertilized by a sperm that has a Y chromosome, a male is formed, but if it is fertilized by an X bearing sperm, a female is produced. Viewing what has been said up to this point, one could easily assume that the Y chromosome stimulates male characteristics. However, the fact is that the Y chromosome plays no role in sex determination; in fact, it is almost entirely devoid of genes. In an anthropomorphic sense, we could think of it as merely a companion for the X chromosome. Therefore, sex determination must involve the difference in the number of X chromosomes in males and females. The question might arise as to how one or two chromosomes can determine the sex of the entire organism. It should be understood that there are genes for both sexes in all of the body cells of both males and females and that the important aspect is any factor that will offset the balance and tilt it in any direction. Bridges found that the off-setting factor is a change in the ratio of X chromosomes to autosomes. The X chromosome will initiate the spark for female production and autosomes for male production. The female stimulation potential of an X chromosome is 1.5 as compared with the male stimulation potential of 1.0 of a haploid set of autosomes. (Winchester, 1958).

In his work on <u>Drosophila</u> melanogaster, Bridges described some of the effects that changing the ratio between X chromosomes and autosomes would have on the sex of the flies. The result of such changes are listed in Table 1. The table illustrated that when the ratio of X chromosomes to autosome pairs is 1:1, normal females are produced. If the number of X chromosomes slightly exceeds the autosome pairs as in 4X:3A, a super female is formed. When the number of X chromosomes is one half, the number of autosome pairs as in 2X:4A, normal males are produced and 1X:3A produces super males. Intersexes are produced when the ratio is intermediate between 1:1 or 1:2 as in a 3X:4A condition. Such individuals would possess both male and female secondary sex characteristics. Normally a large number of genes on the X chromosomes and the autosomes are responsible for determining the sex of an individual. However, the mutation of a single gene is capable of up-setting the original balance and reversing the sex. Although many genes are involved in sex determination, there are certain genes that must be present and with a specific frequency in order to produce a definite sex. (Wagner and Mitchell, 1955).

TABLE I

THE EFFECTS OF CHANGING THE RATIO OF X CHROMOSOMES TO AUTOSOMES ON THE DETERMINATION OF SEX IN *DROSOPHILA* MELANGASTER

Super Female	3X : 2A
Female	4X : 4A
Female	3X : 3A
Female	2X : 2A
Intersex	3X : 4A
Intersex	2X : 3A
Male	1X : 2A
Male	2X : 4A
Super Male	1X : 3A

C. The XO Method of Sex Determination

The XO method of sex determination is found in several orders of insects. This theory was actually discovered before the XY method. It was discovered by Wilson that squash bugs, Anasa tristis, had twenty-two chromosomes in the somatic cells of females, and the eggs had eleven chromosomes in the haploid state. However, a contrasting situation existed in males; they had only twenty-one chromosomes in the somatic cells. Spermatogenesis results in one half of the sperms carrying eleven chromosomes and one half carrying ten chromosomes. The sperms that carried eleven chromosomes had ten autosomes and one X chromosome; the others had ten autosomes and no sex chromosomes. Eggs fertilized by sperms with eleven chromosomes produced females and the ones fertilized by sperms with ten chromosomes produced males. It was stated in the XY method that the Y chromosome does not play any role in sex determination; therefore, it might be assumed that in those animals that exhibit the XO method, that the Y chromosome was lost in the evolutionary development. The Aphids have a rare pattern of the XO method. They illustrate a type of parthenogenesis in which spring and summer eggs are unfertilized and develop into females. They will mate and produce eggs that remain dormant during the winter. These eggs produce females during the next spring. The winter eggs have six chromosomes and produce females with six chromosomes. However, some of the fall eggs will have six chromosomes, two being X chromosomes and some will have five chromosomes, and only one is an X chromosome. The six chromosome eggs hatch into females and the five chromosome eggs hatch into males. (Winchester, 1958).

D. Homozygous and Heterozygous Conditions

Normally among dioecious animals, there is numerical equality between the sexes. Therefore, sex determination is dependent upon a situation in which the chance of producing a male or female is 50-50. For the purpose of illustration, let us suppose that one of the sexes is a recessive homozygote and the other is a heterzygote. If we call the genes of the male M,m and the female gene F,f, there would be two possible gene arrangements. The first possible gene arrangement would be ff for female and Mf for males. In this case, the M is dominant over F. The second possible gene arrangement would be Fm for females and mm for males. In the second case, F is dominant over m. In the first case, all female gametes will be f, but the male gametes will be half M and half f gametes. This implies that females are homozygous and males are heterzygous. The situation is reversed in the second case; females are heterozygous (F or m) and males homozygous (m). This hypothesis has been verified as the result of experiments by C. Correns and E. Witsch. It has been concluded that sex determination is dependent upon a mechanism in which one sex is heterozygous and the other is homozygous recessive. When Oogenesis is completed, all the Oocytes contain an X chromosome but only one half of the spermatids from the same auxocyte will contain X chromosomes. The chromosomal formula for males and females are as follows:

SEX	SOMATIC CELLS	GAMETES
male	2na + XY	50%(na+x) and 50%(na+y)
female	2na + XX	na + x 100%

The symbol "na" represents the autosomes. (Caullery, 1964)

E. Sex Ratio

For the forms of animals in which the males have the XY chromosome arrangement, one might assume that either the X or the Y bearing sperm might be more active and reach the egg sooner than the other or that the egg might be more susceptible to one than the other. However, this is a speculation for which there is no definite proof at the present. Data available at the present indicate that the sex ratio varies from species to species and from race to race. The season, the nature of breeding, order of birth and age of parents will also cause it to vary. Selective mating has been known to change sex ratios. Two pairs of rats from the same litter were bred separately for six generations. Two vigorous stocks were obtained; one was designed as the high ratio and one the low ratio. The rats were imbred for fifteen generations. At the end of this experiment one hundred and twenty-five males to every one hundred females were obtained from line "A." However, eighty-three males for every one hundred females were obtained from line "B."

Evidence indicate that in man the ratio at conception is approximately one hundred and twenty-five males to one hundred females. However, at birth this ratio has changed to one hundred and three males to one hundred females. Other studies indicate that there are several factors responsible for the variation in this ratio. In the United States, the Negro and White populations have a different ratio. Different ratios are also found in other races throughout the world. One cannot be certain if these differences are entirely racial in nature or if they are influenced by environmental conditions under which the different races live. It has been observed that the intra-uterine mortality rate is greater for males than females in all races. It might be assumed that this increased prenatal death of males is due to a lack of parental care and in turn reduces the sex ratio. This simply means that males don't receive as much nourishment as females during the prenatal period. One should accept this information with caution due to the lack of sufficient proof for certain assumptions made. (Burlingame, 1940).

The term sex ratio may be defined in general sense as the proportion of males compared to the proportion of females. In a more specific sense this term can be explained from three different levels. The first is the primary sex ratio and is defined as the proportion at conception. It is the proportion of eggs fertilized by X bearing sperms as compared to those fertilized by Y bearing sperms. The next level is the secondary ratio. This is the number of males born as compared to the number of females born. This is the ratio that is most often observed. The third level is the tertiary ratio which is defined as the porportion of males compared to the number of females at the age of which children become independent of their parents. As was previously stated, most of the present data on human sex ratio refers to the secondary ratio and its percentage of viability. One approach is to examine the viability and mortality rates at various stages after conception. This will give an estimate of the primary ratio and is important because there is no definite method of examining the sex-differential properties of spermatozoa at the present. Until recently, it was thought that the primary sex-ratio was considerably greater than one half. Aborted fetuses were sexed in order to gain this estimate. Calculations were then made to determine what primary sex ratio would be necessary to give rise to the known secondary ratio. There is still much research being done in this area and there are still many questions unanswered. (Caspari and Thoday, 1962).

A colony of Albino rats was started in 1910 at the Connecticut Agricultural Experiment Station, New Haven. This colony was maintained without the addition of outside rats and is one of the oldest in existence today. Of particular interest is the reversal of sex ratio at birth between 1922 and 1960. In the 1922-1933 period, there were more males than females born. During the 1934-1946 period, the ratio was 1:1 but after 1946, the number of females exceeded the number of males. Thus a complete reversal in sex ratio at birth occurred in this colony. (Lester, 1962).

F. Gonadal and Extragonadal Sex Differentiations

The embryological development of the male and female gonds follow separate paths in dioecious animals. In males, the seminiferous tubules are derived from the primary sex cords and the cortex is separated from the medulla by a band of connective tissue, the tunica albiginea, during the seventh week of prenatal life. The mesenchyne gives rise to the interstitial cells, which are very numerous during sex determination. However, these cells regress but reappear in large numbers again at puberty. In females, the primary sex cords and other medullary components regress, and the germinal epithelium give rise to secondary sex cords. The external genitalia and the urogenital sinus are formed from the same primordia in the two sexes, but the internal genital ducts are derived from different primordia. In male embryos, the Wolffian duct gives rise to the epididymides, vasa deferentia and seminal vesicles during the third month. At about the same time the Mullerian duct regresses. The formation of a scrotum, penis, and penile urethra results from fusion of the lobiosctotal folds, the urogenital folds and growth of the genital tubercle. In females, the Wolffian ducts atrophy early in the third month. The fallopian tubes are derived from the upper portion of the Mullerian ducts and the uterus and the upper third of the vagina are formed by the fusion of the lower portion of the Mullerian ducts. The urinary and genital tracks separate in females after the vagina is formed. The development of male sex organs and masculine traits is dependent upon a secretion from the fetal testis. If the testis is removed, the fetus will develop female organs and feminine secondary characteristics. However, if the fetus is castrated in a unilateral manner, one side will develop female organs while the other develops its normal male organs and traits. The secretion from the fetal testis is probably an androgenis steroid produced by the interstitial cells. Female differentiation of the extragonadal sex structures does not depend upon hormones. It occurs in both male and female mammalian fetuses in the presence of gonads. However, androgenic hormones can bring about intersual or masculine development of the urogenital sinus and external genital organs in female fetuses. Mullerian duct differentiation has not been proven to result from androgens. (Penrose, 1961).

G. Gynandromorphs

A very interesting condition was observed in Drosophila melanogaster in which one side of the body was male and the other female. The male and female sections were not always equally distributed. Sometimes only a third of the body was of one sex and two thirds the other. The animals begin their development with two X chromosomes but sometimes during cell division one X gets lost. The portion with the normal amount of X chromosomes becomes female and that which has lost an X becomes male.

Should the following cell divisions be irregular, the male portion would form only a small segment of the total body. Such an animal is termed a gynandromorph.

Another example of gynandromorphism is found in silkworms. The formula for the male worm is XX and the female is XY. In females, a mature egg contains either an X or Y chromosome. A polar body is also formed that contains either an X or Y chromosome. In certain cases the polar body fails to separate from the egg. It remains in the egg and as a result, the egg has two nuclei. Normally, an egg is fertilized by only one sperm because there is only one egg nucleus. However, this particular egg would contain two nuclei and is therefore capable of being fertilized by two sperms. Such eggs are said to be binucleate. As was previously mentioned, all sperms contain X chromosomes in silkworms. The union of a sperm with the X bearing egg nucleus produces male tissues and body organs, but the union of a sperm with a Y bearing egg produces female tissues and organs.

Gynanders are also found in bees, but the exact details of their development are incomplete. It is assumed that the eggs become binucleate due to a failure of the polar body to separate or the fact that it began to develop parthenogenically. Female tissue is formed when these eggs are fertilized by only one sperm. On the other hand, two sperms could enter, one would unite with the egg nucleus and the other one, known as a supernumery sperm cell, would not. Instead of uniting it would form haploid tissue which would be male. The binucleate eggs are usually the results of mutations. (Altenburg, 1957).

H. Sex Reversal

1. Moths

Goldschmidt, in his work with the gypsy moth, Lymantria dispar, found a strain with a tendency to reverse the sexes. He crossed the European and Japanese varities of the moth, Lymantria dispar, and recovered progeny that were mostly intersexes. These insects possessed varying degrees of intermixture between male and female characteristics both in their general external anatomy and their genital structures. He also observed some extreme cases in which the insects began their development with male organs, but later developed female organs. It was discovered that there was a specific time for the development of the sex characters. The antennae appear toward the end of the pupal stage but the gonads appear before the larvae hatch. The male sex organs develop before the female organs. It was suggested that the degree of sex reversal is inversely proportional to the order in which developmental differentiation occurs. The weaker grades of intersexes show reversal only in those parts which are late in differentiating, whereas the stronger intersexes show reversal in those which differentiate early. An insect that begins development as an XY individual will develop as a female under this influence up to a certain turning point. After this point, the development will be controlled by the stronger of the two genes. In moths, the female is the hetorogametic sex. Goldschmidt said that a female factor was carried on the Y chromosome and the male factor on the X chromosome is stronger in the Japanese moth than in the European. Normal XX sons and intersex XY daughters were produced from a cross between European females and Japanese males because the Japanese X partly overcame the European Y. The F_2 progeny included normal sons and daughters. All offsprings were normal when Japanese females were crossed with European males since the European X was not sufficiently strong to overcome the Japanese Y. When inbred, however, the females were all normal, but half the sons were intersexes due to the greater strength of the Japanese X.

2. Crabs

Another case of sex reversal can be observed in crabs, *Inachus*. The male has larger claws and a smaller abdomen than the female. A parasite, *Sacculina* will infest the crab and destroy certain organs by growing strands of tissue through its abdomen. This causes the abdomen to increase in size and take on the appearance of the female and the pinchers are reduced in size. The key to this change seems to be due to the elimination of the fat metabolism. It is not definite, however, if this is the stimulus that initiates sex reversal. (White, 1962).

I. Techniques for Prediction

For centuries man has wanted to be able to determine the sex of his children. Not only has he wanted to determine the sex but he has had the desire to be able to foretell the sex of the children after conception. This was for many years a fantastic dream; however, in 1956 through the achievements of science, it became a reality. This remarkable discovery was made by Dr. Murray L. Barr at the University of Western Ontario. He found that a particular nuclear structure, chromatin body, was present in some embryos and that it stained very dark. The structure was absent from other embryos. Follow-up studies showed that the embryos that possessed this dark staining body always developed into females and the ones without it males. Therefore, in order to predict the sex of the unborn child, the only thing one has to do is to obtain some of its cell, stain them by a designed procedure and make a microscopic examination to check for the presence or absence of the chromatin body. These cells of a living fetus in utera are obtained by a procedure known as "transabdominal amniocentesis." This means that the cells come from the amniotic fluid. Certain cells are known to drop from the fetus and into the fluid. The physician will pass a needle through the abdomen of the mother and remove some of these cells. This is not a recommended procedure because it has, in certain cases, resulted in other complications associated with pregnancy. However, it has also been used to remove excess fluid that is causing pain to the mother. This procedure has enabled scientists to study the sexual development of a fetus before there are ever an external feature of sex present. These external features occur in about the seventh week of development in man. This technique has been useful in studying some of the problems of hermaphroditism. In cases where the individual has organs of both sexes, the physician can examine cells from the cheeks to determine if the chromatin body is present. This will give the true genetic sex of the individual and the physician will know whether or not this condition is chromosomal or hormonal in nature. (Montagu, 1959).

J. Transformer Gene

It was reported by Sturtevant in 1945 that he had discovered the presence of a recessive transformer (tra) gene in Drosophila melanogaster. If this gene occurred in the homozygous condition in females, it would convert them to males. The males in this case were all sterile. However, they had the general phenotypical appearance of other normal males but their testes were rudimentary and did not produce sperms and male hormones. In Drosophila, the male can be distinguished from the female by the presence of sex combs on the legs. The forelegs have a sex comb consisting of a row of bristles arranged like the teeth of a comb, whereas the female lacks this organ. If a superfemale is homozygous for the (tra) condition, she will be converted to a male. However, this male will only have half the normal number of teeth in his sex comb. This is an indication that the superfemales are more resistant to the masculinizing effect of (tra) than are normal females. In explaining the action of (tra) on sexual phenotypes, one may assume that the (+) allele of (tra) directly or indirectly leads to an enhanced activity of the female determining substance produced by the X chromosome genes. This is normally present in double doses in flies. It may also surpress the masculinizing effect of the substance produced by the autosomes. The (tra) gene would be inactive in this respect. Thus in normal females, the masculinizing action of the autosomes would be overcome by the feminizing action of the X chromosomes only in the presence of a (+) allele at the transformer locus. (King, 1962).

K. Number of Genes

It has been generally agreed upon that the sex of Drosophila is determined by the number of X chromosomes in a fertilized egg. The presence of one X produces a male and two a female. However, based on studies made by Bridges and others it has been decided that in a specific sense it is not the chromosomes alone that determine the sex but the balance of genes on the chromosomes. The question at hand is how many genes are involved in the determination of sex. There are two possible approaches to this situation. First, the X chromosome may contain a single gene or several genes that promote femaleness and one of the autosomes may contain a single gene or several that promote femaleness. Secondly, many or all the genes in the X chromosome may determine femaleness and many or all the genes in the autosomes may determine maleness. The effect of any one isolated gene may be small but the entire group may have a powerful effect. Diploid males that had duplications for certain sections of the X chromosome were outcrossed to triploid female in order to distinguish between these two possibilities. Progeny was recovered that had two X chromosomes and a section of a third. They also had three sets of autosomes and some additional fragments; these were intersexes. If an intersex individual has a chromosomal fragment with female potentials and in duplicated state, this individual will be more femalelike than one without the duplication. A similar condition would prevail in the malelike intersexes. The longer the duplication or the more tendencies toward a particular sex are added to an intersex the more like that sex it becomes. To summarize this point, one may conclude that an X chromosome has no single gene, that is, alone responsible for producing a female. The fact is that many genes at different loci on the X chromosome combined their effects and initiate female production. Some sections of the autosomes are neither male nor female determining. Therefore, the problem of the autosomes in this respect has not been completely solved. (Sinnott, Dun, Dobzhansky, 1958).

L. Haploid Males

Another system of sex determination is one in which the females are diploid and the males are haploid. This occurs in certain insect orders such as Hymenoptera, Homoptera and Thysanoptera. The insect in which the phenomenon has been given more attention is the honey-bee.

The best explanation for this was formulated many years ago and is known as "Dzierzon' rule." The rule states that females were produced from fertilized eggs and males from unfertilized ones. There are certain exceptions to this in general; especially in regard to the Hymenoptera. Some species of this order produce females from unfertilized eggs and rarely produce males. After the formation of a polar body, if there is no reduction in the chromosome number, a diploid female may be produced by parthenogenesis. When two polar bodies are formed and there is chromosome reduction, a haploid male is formed. Due to the fact that the former situation rarely occurs in honey-bees, Dzierzon' rule is for all practical purposes valid in this case. When meiosis occurs in haploid males, haploid sperms are produced. However, this is a different type of meiosis from that found in diploid individuals. There are two mitotic divisions but in the first one, the nucleus does not divide and produces a nucleated cell and non-nucleated one. When the nucleated cell divides the second time, it produces two functional sperms. An exception to this occurs in the honey-bee in which only one sperm is functional. Eggs of most Hymenoptera contain haploid nuclei after going through two polar body divisions. If such an egg is fertilized, it developes into a male and if not fertilized it developes into a female. (Sturtevant, 1962).

M. Less Immediate Causes

Certain recent investigations have shown that sex determination may be due to some less immediate causes. Bridges did some important experiments with Drosophila that illustrated this point. In certain instances, a rare phenomenon occurred during gametogensis in which some gametes remained diploid. This is an exception to the general rule which says that gametes are haploid and somatic cells are diploid. In the event that a diploid gamete was involved in fertilization, the resulting zygote possessed a 3n chromosome number. This type of individual is termed a triploid. If two diploid gametes unite, a tetroploid zygote is formed. This type of (polploid) condition is more common in the plant kingdom; however, it does occur in certain animals, especially insects.

Bridges occasionally obtained polyploid or heteroploid Drosophila, which he was able to breed, and cross with diploids. This gave him results similar to the ones in the table on page six.

It can be seen from the table on page six that what really determines sex and its phenotype is the value of the ratio X:na which is 1 for females and 0.50 for males. That is to say, that the sex depends on a certain balance between autosomes and heterochromosomes. (Caullery, 1964).

The haploid nuclei of vertebrates have a strong tendency to become diploid. This is the result of a doubling of the chromosomes without nuclear division known as endomitosis. The chromosome number of parthenogenic haploids is doubled in the process of maturation. The XX chromosome arrangement is characteristic of males in Aves, so the parthenogenetic turkeys at Beltsville, Maryland, are males. Both male and female progeny could be produced by mating these males to an Xy female. The reserve situation is true in frogs, parthenogenic XX are females. (Sager and Ryan, 1962).

N. Origin and Significance of Sex Chromosomes

As one nears the top of the phylo-genetic tree of animals, there is a marked reduction in the occurrence of hermaphroditism. This is an indication that as animals become more advanced, the bisexual phenomenum becomes more firmly established. There arises a great morphological and physiological difference between male and female sex organs. Should intersexes appear at this point, their sex organs are vestigial. They are sterile and can not contribute to the preparation of the species. This makes it manditory to have the sex of each individual decided so firmly that it will develop either as a male or female. This is accomplished primarily by means of sex chromosomes. (Dobzhansky, 1958). In recent years, much research has been done on the behavior of the sex chromosomes during meiosis and mitosis. The results of some of this work have shown that certain variations exist in both the number and structure of the sex chromosomes within a specific group of animals. Therefore, as one approaches the topic of the sex chromosomes and sex determination, he should keep the fact in mind that this is not a stratic phenomenon but that this is subject to several changes or modifications. It should be pointed out that more abnormalities can be found and associated with sex chromosomes than with autosomes. It has already been stated that sex determination is largely due to sex chromosomes. Perhaps the question might arise at this point as to what is the origin of sex chromatin. Some of the cytological evidence gained from recent studies indicate that the sex chromatin mass in somatic interphase nuclei is probably derived from a heteropycrotic segment of a single X chromosome. Some of the autoradiographic studies showed that there are two types of X chromosomes in normal females. One of these appears to be inactive while the other one synthesizes DNA for a long period of time. (Pavan, Chagas, Caldas, 1964).

CHAPTER III

NON-CHROMOSOMAL EFFECTS ON SEX DETERMINATION

A. Hormones and Sex Determination

1. Mammalian Hormones

In vertebrate embryos, the chromosomal make-up initiates the developmental process to proceed either in a male or female direction. However, as the development progresses, it is influenced by several hormones that are capable of reversing the process and directing it toward the opposite sex. An example of this can be seen in twin cattle where one is male and the other female. Certain interconnections between the twin's blood have been known to occur. The male sex organs develop earlier than the female organs. The testes of the male fetus, therefore, start secreting hormones first. The male produced a rare hormone which depressed the secual development of his twin sister. This causes the female to develop into a sterile or intersex-like animal. Such an animal is known as a freemartin. The freemartin is a commercial loss and is not welcomed by breeders among their herds. The hormone effect in cattle and other mammals is different from that in birds. The male hormones are essential to the development of the male characters, but the female hormones will not inhibit them. However, the male hormone may have an inhibiting effect on females during development.

In Dorset sheep, both males and females are normally horned but the horns of the female are much smaller than those of the males. If a male is castrated, its horns will not reach normal size but will only reach the size of female horns. This is an indication that the growth of male type horns is dependent upon the presence of the hormones which are secreted by the testes. Another example of this condition is found in Merinos in which the male has horns and the female is hornless. The female will develop knobs in the depressions where horns ordinarily appear. If a male of this breed is castrated, it will also develop knobs which is an indication of hormone necessity. In breeds such as the Suffolk, Hampshire, Cheviot and Southdowns, both sexes are hornless and have depressions with no knobs. In this condition castration has no effects. (Riley, 1948).

Endrocrine glands other than gonads may also influence the development of male and female sex characters in an unequal manner. In this respect, such glands would function as sex determiners. This is true in particular of the thyroid and pituitary glands. Sexual maturity and the production of eggs can be greatly accelerated in mice by administering extracts from the anterior lobe of the pitutary gland. A month old mouse can thus be caused to produce eggs at a very rapid rate. This is much earlier than what mice normally produce ava. The pitutary gland has a similar effect on the testes. This is a sex stimulator which is essential for the normal functioning of gonads. (Castle, 1940).

Hormones also play an important role in the determination of man. Although the primary sex of an individual is determined at fertilization, secondary sex characteristics don't appear until after birth. These are sexual traits that are not direct parts of the reproductive system.

These differences usually go somewhat unnoticed until the individual reaches sexual maturity. This stage is known as puberty. The boy or girl at this stage is known as an adolescent. At this point, the gonads and other associated glands suddenly increase their secretion or hormones. This causes several changes in both males and females. One marked change is the difference in the rate of metabolism in the two sexes. Male metabolism is about three percent above females at the age of five and continues to rise until it reaches from twelve to sixteen percent greater. However, beyond this point, the metabolic rate in males begins a gradual decrease. This can be observed in females because they have a slower metabolic rate and as a result, they don't utilize all of the energy from their food. Instead, this energy is stored in the form of fat. Since the gonad hormones are essential in the differentiation between the sexes, it is obvious that a damage of distruction to them would cause a change in the sexual development of the individual. Should the testes be removed from a male before sexual maturity, it will show striking effects in the development of the individual. The normal masculine traits will not develop. The voice remains high pitched, resembling that of a female, the beard fails to develop and large amounts of fat are deposited. If the normal development is changed by genes or environmental factors before birth, the young may be born a hermaphrodite. True hermaphroditism (from the Greek god Hermes and goddess Aphrodite) refers to a condition normally present in lower vetebrates. In this condition, sperms and eggs are produced by the same individual. It is a very rare occurrence in man. According to Professor Arey, it is doubtful if such persons can function as both a father and a mother. The internal sex organs are imperfectly developed and the external ones show both male and female characteristics. Most of the so-called hermaphrodites are actually false hermaphrodites. They have gonads of one sex but the external organs tend to resemble those of the opposite sex. The testes of a male false hermaphrodite are undescended and the external organs are female-like. This may be considered a female during childhood but at puberty male secondary sex characteristics begin to appear. In females false hermaphrodites overies are present but undeveloped. The external organs are male-like. During childhood, this individual may be considered a male but developed female secondary sex characteristics at puberty. Those persons should not be regarded as sex reversals, because there is no proof that true sex reversal takes place. (Colin, 1946).

2. Bird Hormones

Another example of hormonal influence on sex determination is found in chickens. Only the left ovary matures and the right one remains vestigial in female birds. Should the left ovary become diseased or destroyed, the right one will develop into a testis and produce male hormones. These hormones will in turn reverse the sex of the organism. These can father chicken hens. This has been experimentally done. The secondary traits of vertebrates are influenced by hormones. This is illustrated by the tail feather pattern in chickens in which males normally have curved tail feathers and females straight ones. Curved tail feathers are also found in castrated birds. This evidence points to the fact that female hormones surpress the curved feathered condition. (Crow, 1960).

In vitra, results have shown that Mullerian ducts of the chick embryo undergoes evolution as a result of androgen activation of an intracellular proteolytic enzyme specific to the duct. It is believed that androgen from the embryomic gonads moves to the Mullerian ducts and determines the formation of the proper enzymes that control the evolution of the ducts. The left female duct is stablized by the effects of Oestrogen. (Hamilton, 1962).

B. Environmental Determination of Sex

1. Bonellia

Only the general potential of sex is determined by the chromosomes in some instances. The environment controls the differentiation of the sex phenotype irrespective of genotype. This condition is illustrated by Bonellia viridis. This is a small worm that is most often associated with the Annelids. It is sometimes placed in a separate phylum, Echiuroidea. These animals show extreme cases of sexual dimorphism. The female is about one inch long and has a very complex anatomical organization. The males are very small organisms and have degenerate organ systems. They resemble cilates and live as parasites upon females. As the eggs of those worms develop, some settle to the bottom of the water and others become attached to the proboscis of a mature female. The ones that settle to the bottom become females and those attached to the proboscis of a female become males. The male fertilizes the eggs. If the controlling female host is separated from the parasite worm, an intersex is produced. It is believed that the female produces some type of hormone which initiates maleness in the attached larva. As a result of this hormone, the environment which is the body of the host is male directing for this larva. The important thing to nature in this case is the fact that there is no internal factor of the larva that direct maleness. The male directing force comes from the external environment. Sex determination of this type is said to be nongenetic. In cases where sex is determined by the environment, a genetic result is obtained which is beneficial. The manner in which this process occurs insures that there will always be some males and some females. This method has a disadvantage in that the sexes produced are usually out of proportion. This type of sex determination has been restricted to the invertebrate animals and vertebrates have a more stable method of sex determination. Chromosomes follow a regular pattern of distribution in gametogenesis and therefore, represent a more stable method of sex determination. (Garder, 1964).

2. Protandry

Another example in which the environment determines sex involves a phenomenon known as protandry. A protandrous animal is one that begins life as a male, but later develops into a female. There is no sex differential of chromosomes since this is the general pattern for these particular species. One common representative of this group is the marine mollusc, Crepidula. This is a slipper shell. The rate of change from male to female is controlled by the environment. If a male is able to find a female for mating purposes, he will remain a male for a long time. However, those males that are unable to mate quickly change into females. Protandry is very common among the molluscs. It occurs in oysters, ship worms and the oysters of the pacific coast. This condition is also found among Virginia species of oysters but permanent males and females are also found. It was discovered by Coe that the change from male to female occurs so early in the life cycle of Tereda that about ninety percent of the population is females. However, there are enough males to fertilize the large number of eggs produced by the females. Rare cases of protandry are known to occur in vertebrates such as tunicates and amphibians. The toads have a pair of potential ovaries, known as Bidder's organs. If they are removed by some agent, these organs will enlarge and become functional. The toad will become a female. (Dobson, 1956).

3. Environmental Controls

After having read the preceding sections of this paper, and realizing that sex determination is controlled by a combination of chromosomes, hormones and environmental factors, it would appear that one could alter these factors and divert the course of development to determine the sex of the offspring at will. Since the sex that will normally develop depends upon whether the egg is fertilized by an X or Y sperm, the only problem, it seems, is to eliminate the undesired sperm. At present, the most logical approach to the problem is to find some particular chemical with which to treat the sperms that will be deposited in the vagina. This chemical should be able to inactivate X bearing sperms if a male is desired and Y bearing sperms if a female is desired. This seems very simple in theory but so far, no one has been successful in securing a practical method of applying it. To some individuals, it probably seems useless to control the sex of unborn progeny. However, there are several situations in which this could be an asset to our society. For example, the production of a large number of males is less in chickens because they don't lay eggs. It is not easy to distinguish between male and female chicks until about the third or fourth day after hatching when testes develop. At this time, the excess males can be disposed. The ideal technique would be one by which this could be determined before incubation, so that female hormones could be injected in the potential male eggs. At the present, it seems that genetic males will develop into phenotype females only because they have a temporary excess of female hormones over the natural male hormones. In a short time the female hormones are exhausted and the male hormones again control the development. These chicks will revert to males. The only possible way to solve this problem is to surpress the entire male endocrine system. This, however, has not been successfully accomplished and it is an area in which much research is being done. (Burlingame, 1940).

CHAPTER IV

CONCLUSION

The writer summarizes this report by pointing out the fact that the differentiation between the sexes in an individual is dependent upon several factors. Basically, sex is determined at the time of fertilization. In most species, it depends upon the chromosomal makeup of the sperms since all normal eggs of these species would have the same chromosome arrangement. There are a few species in which this situation is reversed. However, it should be remembered that even though the chromosome arrangement of the embryo is established at fertilization, it is effected by the total environmental factors in which it develops. It was stated previously that each individual contains a pair of sex chromosomes. However, there are many alleles at different loci that contribute to the determination of sex. Any arrangement or disruption of these alleles could have a definite effect on the sex of the organism. The distinction between maleness and femaleness depends upon a very delicate balance. This balance can be offset by mutations, by insufficient amounts of the proper factor. This means that even though an organism begins its development as one sex, it is possible to develop primary and secondary traits of the opposite sex. Therefore, one can not confine the determination of sex to any one factor alone.

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