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The Genetics of Inherited Abnormalities in Livestock

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1. Introduction

During the last thirty years there has been much knowledge accumulated and published in the science of genetics. The older definition of a gene as a basic unit of inheritance has now been modified. One of the most significant discoveries in recent times, that led to a re-definition of the gene was that of Watson and Crick in 1953. These authors defined a gene in terms of DNA (deoxyribonucleic acid) and DNA has today been universally accepted as the biochemical unit through which inheritance is accomplished.

A phenotype is dependent on two or possibly three major factors namely, the genotype consisting of a wide variety of genes, the environment in which the genes are expressed and interactions between the genotype and the environment. Heredity provides the basic specifications, the environment both internal and external provides the wherewithal for fulfilling these specifications.[69]

2. Abnormalities in general

Abnormalities appear in various forms, different degrees of expression, combinations with other abnormalities through different pathways and modes of origin. If one follows the development stages of an organism from the zygote to maturity, defects or death could occur at any stage of development such as during fertilization or shortly thereafter, during embryonic growth, birth or during postnatal development. If at any stage the animal dies, the abnormality could be termed a lethal abnormality.

Abnormalities and consequently death could occur due to the action of genes when they are referred to as lethal genetic abnormalities. On the other hand abnormalities that result in death may arise due to injury, poor nutrition, climate or the ingestion of poisons when they may be called lethal environmental abnormalities. Similarly, an abnormality where the animal is at some disadvantage but survives, could be called a non-lethal abnormality (taillessness, dwarfism, etc.), and if the abnormality has a genetic component, the genes may be termed non-lethal genes.

3. Whether heredity or environment

It is important to ascertain whether an abnormality that arises for the first time is genetic or non-genetic. If it is genetic it would be eventually necessary to identify its exact mode of inheritance and find out what types of genes are involved. This however is sometimes a very difficult exercise that may take time, and still provide inconclusive results. Even when the abnormality is non-genetic, pinpointing the exact reason for the abnormality is difficult. The difficulty of correct identification of the abnormality is increased further when the environment mimics a genetic abnormality. In case of arthrogryposis for example, the ingestion of toxins, such as those found in lupines[7,72] have resulted in abnormalities similar to the arthrogryposis condition

which is genetic.[29] A type of hereditary congenital flexed pasterns was reported in an inbred herd of Jersey cattle by Mead *et al.*[57] These authors suggested a genetic and a non-genetic mode of inheritance for the same defect, both types having similar phenotypic manifestations.

The classification of an abnormality into genetic or non-genetic is further complicated by genotype x environment interactions. Magee[69] reported one such instance involving scrotal hernia in swine, where the interaction was between the genotype and maternal effect.[69] Among Hereford cattle, cancer eye is common whereas in other breeds such as Charolais and Charbray which have white faces the defect is uncommon.[48]

When a defect occurs in a commercial or a breeding flock for the first time, one is often interested in finding out whether it is genetic or non-genetic. Although one cannot ascertain its exact origin with a very great deal of certainty, some preliminary observations are useful in shedding some light on the problem. In general, a genetic or hereditary basis is indicated, under the following conditions:

1. The defect occurs independent of environment. This may be taken as a case where genotype x environment interactions are minimal and similar defects are seen to occur everywhere.
2. When similar phenotypes have been identified in the literature and large enough samples have indicated a genetic basis.
3. If the defect is confined to one breeding group, usually a sire or dam and their progeny. This observation is a fairly reliable measure as to whether the abnormality is genetic.
4. If inbreeding tends to increase the frequency of occurence, a genetic basis is suspected. Inbreeding does not create genetic abnormalities but just helps to show them up.

On the other hand an environmental basis is indicated under the following circumstances.

1. The defect occurs in relation to a particular environmental factor, and when it could be corrected by providing the necessary conditions.
2. If it occurred following a period of stress and corrected itself when the stress period was over.
3. If it had been previously demonstrated or reported as being due to a toxin, injury, disease, nutrition or any other non-genetic component.
4. If it was not responsive to inbreeding and did not conform only to certain breeding groups or lines.

Abnormalities whether they are genetic or non-genetic, may go completely undetected and never investigated when defective animals are born dead. Often in commercial herds neither is the dead foetus examined, nor is it subject to a post mortem, instead it is buried or burnt as the dead animal is an economic liability. No effort is made to look through breeding records and come to some conclusion about its cause unless the condition recurs.

3.1. The origin of genetic defects

Any genetic defect must come into a population initially through a mutation. Mutations occur at the level of the gene- 'gene or point mutations', or at the level of the chromosomes- 'chromosomal aberrations'. After the re-discovery of the gene by Watson and Crick,[70] it is now believed that the hereditary information is contained in the base sequences along the DNA chains. Changes that occur in the molecular structure of the DNA (like a loss or gain of a base) base pairing sequences that lead to new metabolic actions compared to the original action, is a gene mutation. Jacob and Monod[39] put forward their theory of the operon in which a regulator, operator, promoter and structural genes, consisting of DNA base pairs were recognised. A change in any of these gene base pairs would also be a mutation in the present context. Mutations change genes defined by their physiological action; for the most part these would be changes in the cistrons and operons of molecular genetics.[68] Similarly entire chromosomes or parts thereof may be subject to changes, in structure or arrangement. These are referred to as chromosomal mutations.

Mutation rates are dependent on the kinds of alleles, external and genic environmental factors and in natural environments the rate is about 10^{-5} or 1/1,000,00.[58] Sinnott *et al*[63] refer to the work of Dobzhansky and Spassky who estimated the lethal mutation rate in *Drosophila melanogaster* to be 10^{-5} per gene per generation. Haldane[31] reported that the mutation frequency for haemophilia was between $1x10^{-5}$ and $5x10^{-5}$ per generation. Higher rates of mutation have been reported for certain other characters such as neurofibromatosis in man, 10^{-4}.[58] Table 1 gives a summary extracted from Sinnott *et al*[63] for some characters and their mutation rates in man.

3.2. Genes and their involvement

There are many kinds of genes that affect a phenotype. This paper is written with a particular emphasis on qualitative genes, or genes affecting those traits that can be characterized rather than measured. Qualitative traits are also traits that are influenced by a few genes or that are simply inherited. Genes affecting qualitative traits generally show dominance, recessiveness or incomplete dominance in the phenotype. Genes could conveniently be divided into 3 groups (*a*) major genes which determine to a large extent the expression of the phenotype (*b*) contributing minor genes, which have less significant effects on the phenotype and (*c*) modifiers which could collectively modify the phenotype.

TABLE 1. Approximate rates of mutation per million gametes of some genes in man (After Neel and Schull).

	Disease or abnormality	Rate
Autosomal dominants	Epiloia	10
	Achondroplasia	42
	Pelger's anomaly	80
	Aniridia	5
	Retinoblastoma II	23
Autosomal recessives	Micropthalamos	15
	Albinism	28
	Colour blindness (total)	28
	Infantile amaurotic idiocy	11
	Ichthyosis	11
Sex-linked recessives	Haemophilia	35

Source—Sinnott *et al* (1958).

Genetic defects are more often of a recessive type.[48] In such a situation theoretically the individual showing the abnormality in the phenotype must show a double recessive genotype (bb). The heterozygotes (Bb) and homozygous dominant (BB) types will not usually show the defect. Whenever a defective offspring is born and an autosomal recessive inheritance is established, both parents are automatically identified as carriers. However, even in a carrier (heterozygote) by carrier mating a defective offspring will result only 25% of the time.

Dominance in some instances may be responsible for genetic defects, and the phenotype is usually expressed both in the heterozygote and homozygote. These defects are often semi-lethal and gene frequencies can be quickly lowered, through selection.

Appendix 1 shows a partial listing of genetic abnormalities in Cattle, Sheep, Goats and Swine from the literature.

3.3. Gene Penetrance

When a gene fails to manifest its expected effect in the phenotype it is referred to as being incompletely penetrant.[48] The term penetrance applied to an individual can take on values of either 0 when the defect is not shown, or 1 where the defect is shown. However, when penetrance is applied to a population, it can take on values ranging from 0 to 1. It follows from this discussion that whether a genetic defect is of a dominant or recessive type its expression in the phenotype is again dependent on the level of gene penetrance. Modifier genes as well as other genes in the background genotype are important regulators of penetrance.[28]

Another word often used conjointly with penetrance is expressivity. Expressivity applies only to a gene system that shows penetrance and relates to the degree of expression of a character. For example, Shupe *et al*,[62] reported an investigation of a skeletal congenital malformation which showed variable expressivity, believed to be hereditary in origin, among Hereford cattle. In arthrogryposis affecting Charolais cattle the limb defect is often associated with a cleft palate, which then refers to the expressivity of the defect.[5,6,49,53]

4. Characterization of genetic defects

Gene defects could be categorised differently from the normal approach of classification taking into account, the type of qualitative gene involved, and factors that make elimination of the deleterious gene more difficult. Using these bases, the following classification was developed.

1. Genetic defects that are recessive, autosomal and show complete penetrance.
2. Genetic defects that are recessive, autosomal and show incomplete penetrance.
3. Genetic defects that are recessive, autosomal, show incomplete penetrance and heterozygote advantage.
4. Genetic defects that are dominant in effect with complete penetrance.
5. Genetic defects that are dominant in effect with incomplete penetrance.
6. Sex linked recessive or dominant defects.
7. Defects incompletely dominant that show some expression in the heterozygote.

This report will consider only the first three kinds as a majority of genetic abnormalities are of a recessive type. The methods by which the frequency of the defective gene could be reduced which are discussed in this report will in general apply to recessive inheritance.

4.1 Selection against a recessive gene

Complete selection against a recessive gene which is responsible for a genetic abnormality is difficult to achieve as recessives are usually hidden in the heterozygote. Falconer[17] showed that (1) selection was most effective at intermediate frequencies of the defective recessive gene and became least effective when the gene frequency was large or small and (2) selection was ineffective when the recessive allele was rare. Lasley[48] stated that discarding or culling all homozygous recessive individuals in a population reduces the recessive gene frequency but does not eliminate it.

It becomes necessary at this point to digress from a purely qualitative basis into population genetics, which relate to gene frequencies. The theoretical basis for the study of populations arises from the Hardy-Weinberg law, and Falconer[17] defined it as follows: in a large random mating population both gene frequencies and genotype frequencies are constant from generation to generation in the absence of migration, mutation and selection, and the genotype frequencies are defined by the gene frequency. Assuming that the Hardy-Weinberg law operates and q is the frequency of the recessive gene in a population then (1-q) = p = frequency of the dominant allele in the population. The genotypes in the next generation will be as, $p^2 + 2pq + q^2$, where,

p^2 = Dominant homozygotes (AA)
$2pq$ = Heterozygotes (Aa)
q^2 = Recessive homozygotes (aa)

Table 2 which is presented subsequently, demonstrates that even though the frequency of a lethal recessive gene is very low in a population, there are sufficient numbers of heterozygotes (Carriers) still carrying the deleterious gene. Table 2 was constructed assuming that the Hardy-Weinberg equilibrium operates.

TABLE 2. Relationship between gene frequency and % carriers.

Frequency of the recessive gene (q)	%Heterozygotes or carriers (2pq)
0.5	50%
0.3	42%
0.2	32%
0.1	18%
0.05	9.5%
0.01	1.98%
0.005	0.995%

Table 2 demonstrates that when 1 out of every 100 or 0.01 is abormal 18% of all animals are carriers. Similarly, when 1 out of every 10,000 is abnormal, 2% are carriers.

Now let us assume that the frequency of arthrogryposis in Charolais cattle was such that every 1 in 100 was crippled. Assuming that penetrance is complete, the frequency of occurrence was $q^2 = 0{\cdot}01$, therefore $q = \sqrt{0.01} = 0.1$ Thus the frequency of the normal allele p = (1-q) = 0.9. At equilibrium, the heterozygotes in the population will have a frequency of $2pq = 2\ (0.9 \times 0.1) = 0.18$. Thus the ratio of heterozygotes: recessive homozygotes is 0.18: 0.01 or 18:1. In other words, heterozygotes are 18 times more frequent than the defectives. As the frequency of the defective gene becomes smaller the frequency of the carriers relative to the frequency of those showing the defect will increase.[63]

Thus far in the discussion we have considered situations where selection is 100% effective against a recessive homozygote or where S = 1. Falconer[17] stated that "S" the selection coefficient denotes the strength of the selection or the proportionate reduction of the genetic contribution of a particular genotype, compared with a standard genotype usually the most favoured. The selection coefficient S = Q, when all individuals and genotypes concerned survive and reproduce.

Opposed to the selection coefficient is the fitness or the adaptive value 'W' (Sinnott *et al*[63]) given as 1 - S. Now when a genotype is lethal or sterile and selection is is 100% effective, then S = 1 and W = (1—1)= 0. Thus depending on the strength of selection, 'S' can take on values from 0 to 1.

Table 3 has been obtained from Sinnott *et al*[63] and shows the effect of complete selection against recessive trait.

Assuming that the frequency of a recessive gene in a population is 0.5, S = 1, there is a complete selection against the recessive defect, the Hardy-Weinberg equilibrium is valid and heterozygotes are twice as numerous as the recessive homozygotes, the original recessive gene frequency of 0.5 is halved in 3 generations but the carrier (heterozygotes) are 6 times more frequent as the homozygous recessives. After 9 generations of selection the original recessive gene frequency is reduced to 0.1 at which time heterozygotes are 18 times more frequent than the recessive homozygotes. The values demonstrate that as the frequency of a defective gene decreases, the heterozygotes (carriers) become more frequent, selection is less effective, and it takes a long while to reduce the frequencies.

TABLE 3. Effects of complete selection against a recessive trait.

Generations	Gene frequency (q^1) 1,2	%Recessive Homozygotes (q^2)	%Heterozygotes (2pq)	%Dominant Homozygotes (p^2)
1	0.500	25.00	50.00	25.00
2	0.333	11.11	44.44	44.44
3	0.250	6.25	37.50	56.25
4	0.200	4.00	32.00	64.00
5	0.167	2.78	27.78	69.44
9	0.100	1.00	18.00	81.00
10	0.091	0.83	16.53	82.64
20	0.048	0.23	9.07	90.70
30	0.032	0.10	6.24	93.65
40	0.024	0.06	4.76	95.18
50	0.020	0.04	3.84	96.12
100	0.010	0.01	1.96	98.03

Source—Sinnott *et al*[63]

1. Formula used to calculate q_1,[17]

$$q_1 = \frac{q^2(1-S) + P_q}{1-Sq^2}$$

When S = 1,

$$q_1 = \frac{P_q}{1-q^2}$$

Where, q_1 = new gene frequency
q = original recessive gene frequency
p = original dominant gene frequency
S = Selection coefficient

2. Formula used to calculate q_1,[48]

$$q_1 = \frac{q}{1-(n \times q)}$$

Where n = number of generations

4.2 Selection against a recessive with incomplete gene penetrance

Thus far we have dealt with theoretical descriptions in populations where selection for a recessive defect is complete, due to possibly lethality and complete penetrance of the defective gene. For the purpose of our discussion the selection coefficient 'S' could be equated to penetrance (P) and if S = 0.1 the level of penetrance would be 10%. We have also seen the difficulties that arise in reducing recessive gene frequencies when, P = S = 1. The difficulty in controlling gene frequencies is further aggravated when penetrance of the defective gene is incomplete. The effectiveness of selection in large breeding groups is proportional to the level of penetrance; if penetrance is low selection against a recessive defect would naturally be less effective than if the intensity of selection or penetrance approached unity.

Sinnott *et al*[63] showed results which demonstrated some of the additional difficulties that may arise due to partial selection or incomplete penetrance (table 4).

TABLE 4. Effects of partial selection (due to incomplete gene penetrance) against a recessive trait on the frequency in %, of the individuals homozygous for the recessive gene.[1]

Generations	S=P=1	S=P=0.5	S=P=0.1	S=P=0.01
1	1.00	1.00	1.00	1.00
10	0.25	0.46	0.84	0.98
20	0.11	0.26	0.71	0.97

Source—Sinnott *et al*[63]

1. Table values calculated assuming 1% homozygous recessive individuals or q = 0.01.

When penetrance was complete 10 generations were needed to reduce the gene frequency to a quarter of the original value. When penetrance was 50%, 20 generations were needed to reduce the the original gene frequency to a quarter of its original value and selection was very ineffective in bringing about a change in gene frequency in 20 generations, when penetrance was 10% and 1%.

Incomplete penetrance may also be associated with heterozygote advantage[5] and if it be the case, selection for the heterozygote is obvious and this will help to maintain the frequency of the recessive defective gene, stationary in a population under natural selection. If heterozygote advantage is observed in economic and production characters the defective gene frequency will again be maintained at above normal levels in commercial populations, due to the advantage gained through artificial selection.

One aspect that we have assumed in the discussion so far is the idea of a large random breeding population, a prerequisite for the Hardy-Weinberg law to be operative. However, in commercial herds random mating is not practiced instead, specific breeding plans are carried out and animals selectively bred. Furthermore, the breeding populations we would deal with are usually small. These two factors are therefore confounded in this discussion and looking at selection with the element of random breeding removed would be a more exact approach, although it is difficult to accomplish.

5. Methods of identification of recessive defects

There are many methods available for the detection of recessive abnormal inheritance in domestic livestock. Some of these methods are restrictive in the sense that certain previous records such as pedigrees, are needed, while others involve planned breeding and whether or not it should be practiced to identify a carrier of a genetic defect depends on factors, such as the attitude of the breeder, the severity of the defect and the frequency of occurrence.

5.1 Pedigree analysis

A pedigree is a record of an animal's ancestors that are related to it through its parents. A pedigree to be useful in detecting an inherited defect must contain all necessary information, such as numbers identifying the animals, the condition of all progeny born and detailed descriptions of any abnormalities encountered. A pedigree is particularly useful in tracing the sire (s), dam (s), animal (s), or breed (s) that may have introduced the defective gene into the population. In the study of recessive

gene inheritance through a pedigree the following should be borne in mind, (1) a recessive gene must be independently introduced to the maternal and paternal sides of a pedigree if ever a defective offspring results. (2) Common ancestors appearing on both the sire's and dams' side of the pedigree are often responsible for the introduction of the recessive gene (3) whenever a defective offspring is both parents automatically become carriers.

The pedigree presented in chart 1 is taken from a population of Charolais and Angus cross bred cattle from the University of Alberta herds in Kinsella, Alberta. A pedigree record in this instance was used to determine how the defective arthrogryposis gene was introduced into this pedigree. Assuming that the defective gene must be introduced independently to the sires' side and the dams' side in the pedigree, let us see whether there are any common ancestors. Sire ≠ 3 is a common ancestor being the maternal grand sire of ≠ 13 and ≠ 15 and the sire of ≠ 14. Furthermore, this particular defect, namely, arthrogryposis was peculiar to the Charolais breed and sire ≠ 3 was pure Charolais which further suggests that this sire may be the one responsible for the introduction of the defective gene.

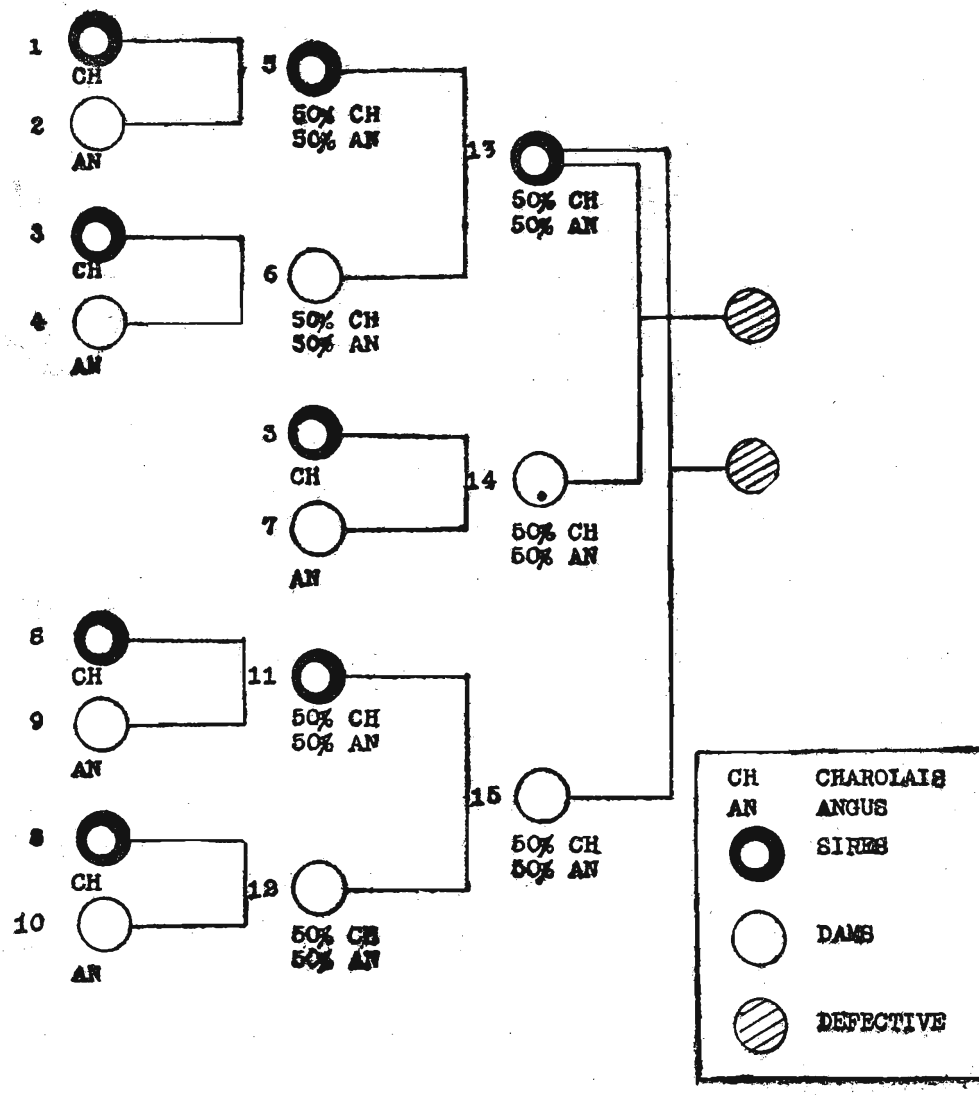
A pedigree record can therefore suggest how the gene was introduced and through which animal but cannot always recognise the mode of inheritance.

5.2. Mating of a phenotypically normal sire (which may be a carrier) to known carrier females

A homozygous dominant genotype (AA) would produce gametes of only one type, and when bred to carrier females would produce all normal phenotypes, of which half will be carriers and phenotypically normal and the other non-carriers and genotypically clean. If on the other hand if the male is a carrier that is a heterozygote (Aa), twenty five percent (0.25) of the offspring will be double recessive (rr) and show the defect, provided P = 1. The probability of an individual being normal is 0.75 and the probability of all n offspring being normal is then $(0.75)^n$. At P=0.05, one would expect at least 10 normal offspring $0.05 = (0.75)^{10}$ to prove that the sire is clean and at p=0.01 one would need 15 normal offspring $0.01 = (0.75)^{15}$ to prove the sire is genotypically clean.[69]

Certain practical limitations are obvious in this method, when applied to species such as cattle. A sire can be sufficiently proven to be a non-carrier as it could be bred to many dams but one would have to use a dam's entire lifetime to ascertain whether she is a carrier of a defective gene. Secondly, one could do this test only if a nucleus herd of carrier cows was available.

Pedigree Chart - 1



5.3 Sire daughter matings.

If a carrier sire is bred to non-carrier dams, half its progeny would be carriers. If all or a random sample of daughters (progeny) are bred back to the sire and one defective offspring detected, the sire becomes proven as a carrier. However, about twice the number of sire x daughter matings are necessary to reach the same levels of probability as when known carrier females are used.[69] A very serious disadvantage in using this procedure is that, sires are too old when the offspring of their daughters are obtained, especially among species that have long generation intervals.

5.4 Mating a sire/dam to a double recessive sire/dam

The procedure applies only to situations where the defect is semi-lethal and there is no associated reproductive failure. It can be used to detect carrier sires or dams. In this method one parent is always homozygous and recessive (rr). If the other parent is a carrier and $P=1$, then 50% of the offspring would show the defect. If on the other hand, the other parent was normal the defect would not be seen in any of the offspring. The probability of all offspring being normal is then $(0.5)^n$. If four or five offspring from such a mating combination were normal, $P=0.06$ and 0.03 respectively or the chances are 94% or 97% that the animal in question is normal. This is a very powerful test but has its limitations.[69]

6. Why do recessive genes persist in populations?

Recessive genes that are responsible for certain undesirable abnormalities appear to persist in populations sometimes at stationary frequencies and at other times, at above normal frequencies. I will now attempt to theorise on why such genes persist in populations inspite of their adverse effects.

6.1. Recurrent mutation

Mutations result in a change in gene frequencies from one allelic state to another at a prescribed rate. The rate of mutation was determined to be around 1×10^{-5} per generation[58] and based on this value, mutations were classified as rare events.[23] If a mutation was of a recessive and disadvantageous type selection, complete against the recessive state, and there was no heterozygote advantage, the frequency of the recessive gene must reduce over time. However, if the mutation involved an area on the DNA or chromosome which tended to be more mutable than other loci, the same disadvantageous recessive phenotype may once again be introduced into the population due to the recurrent nature of such mutations.

Since recurrent mutation is a weak force in changing gene frequencies compared with say selection, one cannot expect deleterious recessive gene frequencies to be maintained at high and stationary levels in breeding groups by this process.

6.2. Frequency dependent selection

Frequency dependent selection in its simplest defunction means that a gene or genotype is selected when rare and selected against when common.[58] Its fitness therefore depends on gene frequency. Frequency dependent selection is seen to be operative in the production of balanced polymorphisms in mimicry[23], and in the esterase 6 locus in *Drosophila melanogaster*, as reported by Kojima and Yarborough.[46] On this basis a recessive gene which may be a disadvantage at high frequencies but an advantage at low frequencies may be maintained at a stationary frequency in populations. However, for this equilibrium gene frequency to be maintained we must presume that the recessive gene in question could confer some selective advantage to another genetic system associated with fitness, only when it reaches a low frequency. Furthermore, although frequency dependent selection can establish a low and stationary frequency for a recessive gene its potential in maintaining the frequency of a recessive at a high frequency is questionable.

6.3. Heterozygote advantage

Heterozygote advantage is one of the most effective methods whereby defective and recessive genes are maintained at either stationary or above normal frequencies in populations. Fisher[22] stated that a single factor may be in a stable equilibrium under selection if the heterozygote has a selective advantage over both homozygotes. A classical case of heterozygote advantage is seen in the instance of sickle-celled anaemia in human populations. The disease is controlled by a recessive gene and when homozygous causes anaemia and is usually lethal.[1] Heterozygotes also show the sickling trait in the red blood cells and are slightly anaemic under low oxygen tensions.[2] In spite of the fact that recessive homozygotes suffer from a lethal disease, the heterozygotes and consequently the lethal gene is common in certain regions of the world where malaria is prevalent. Allison[1] stated that the sickling trait confers marked immunity towards malaria. Thus, as the heterozygotes are at a selective advantage, the defective gene frequency appears to be stationary in such populations, and balanced blood type polymorphisms established.[23]

Many experiments were also reported by Dobzhansky[13] on *Drosophila pseudoobscure*. The first was in respect to the character's arrow head AR/AR and pike's peak PP/PP. The selection of the AR/PP heterozygote was favoured. In a second case the standard St/St, and Charicahua Ch/Ch loci inversions could be cited. At 28°C to 30°C the average longevity of the St/St homozygotes was greater than either the Ch/Ch or Ch/St types. However, at 0-4°C there was a distinct advantage in longevity for the heterozygote (Ch/St).[58]

In the recessive genetic defect affecting Charolais cattle, namely, arthrogryposis Berg and Goonewardene[5,6] showed that heterozygote advantage in dams was one reason for the persistence of the defective gene at a high frequency in certain cross,

bred Charolais populations. An arthrogryposis carrier dam population was compared with a control population consisting of dams with similar breeding, and managed under similar conditions. Fertility as measured by the number of successful calvings was better in the arthrogryposis carrier herd. Longevity was also better among carrier dams compared with the control. Heterozygote advantage pertaining to a primary fitness character is therefore of great importance in maintaining recessive and deleterious gene frequencies stationary in certain breeding groups. Lerner[51] cites many examples where heterozygote advantage has been recognised.

6.4. Lack of penetrance and incomplete selection

In many instances a defective gene cannot be easily removed from a population due to incomplete penetrance. In extreme situations there could be zero penetrance, in the recessive state and if animals concerned reproduce normally, all their F 1 progeny would be carriers (assuming that one parent was proven clean). Consequently, the defective gene will be at a high frequency in these populations, especially if the recessive homozygote was a sire that was used extensively in an initial breeding program. Evidence to support the existence of homozygous recessive arthrogrypotic Charolias sires, was reported by Goonewardene and Berg[29] and two case histories in support of the above will be discussed.

A particular sire referred to as (A) was mated to 3 of its daughters in the same year and 3 arthrogrypotic calves resulted. This was the first glimpse of evidence to suggest that this particular sire may have been a recessive homozygote. If sire (A) was a carrier in a true sense (heterozygous) only half its daughters would be carriers and if mated back to its daughters only 25% would be defective. Although the numbers involved are insufficient for a statistical analysis there is room to believe that sire (A) was a double recessive carrier.

A more positive example of homozygosity among sires was reported by a farmer in the province of Alberta in Canada. During the spring of 1970, seven cases of arthrogryposis were observed. While examining the history and breeding records in this herd, the introduction of the defective gene was traced to a pure bred Charolais bull (C) purchased in 1968. This bull was bred to a number of non-Charolais dams mainly Shorthorns the resulting progeny being half Charolais, Shorthorn crosses. In 1971 a full Charolais bull (D) was purchased and used on some yearling and 2 year old heifers, which included among them 15 half Charolais cross daughters of bull (C). In 1972 a total of 32 calves were born through sire (D), 15 of which came from the half Charolais daughters of sire (C). Of these 15 calves, 8 were normal and 7 crippled (positive lesions of arthrogryposis). This approximates closely to a 50 : 50 ratio of normal : crippled calves.

Assuming that the defect was conditioned by a recessive gene pair, both parents must be at minimum carriers (heterozygotes) to drop a crippled calf. All of the half Charolais daughters of (C) would be carriers only if one parent were homozygous recessive. It would appear very likely that bull (C) was the double recessive parent as the defect is unlikely to come through non Charolais dams that were bred to (C). A ratio of 1 : 1 normal: defective calves is expected in a test cross where a heterozygote is bred to a recessive parent. When the daughters (C) were crossed to sire (D), 7 of the calves born were defective. The observed ratio indicates that sire (D) was also a homozygous recessive carrier of the defective condition. If sire (D) was heterozygous, only 25 % of the calves would be crippled provided penetrance was complete. An interesting observation was that sire (D) had very weak front legs and barely able to stand and walk around. The progeny from the daughters of bull (C) bred to bull (D) also had weak limbs at birth which corrected itself after 2-3 weeks.

6.4.1. Dominance modification

Fisher[20] in his classic paper titled "the possible modification of the response of the wild type to recurrent mutations" stated that under experimental conditions, mutant types which had been kept as stock for several generations had been observed to show their mutant peculiarities in a materially lower degree than at first appearance. This observation was clarified by the fact that the effect of a gene can be varied by changes in the rest of the hereditary material and consequently that they are susceptible to selection. Fisher's[20] experiments showed that it is not the recessive mutant gene that is modified instead, the other genes involved in the expression of the phenotype are modified through selection and thereby dominance in the phenotype is achieved. A similar phenomenon appears to operate with respect to arthrogryposis a recessive genetic defect in Charolais cattle. Due to the accumulation of favourable modifier genes the defect has been almost completely suppressed in the phenotype among certain pure bred Charolais bulls. However, among cross bred Charolais animals which do not have the correct sequence of modifier genes selected out, the defect is seen clearly and gene penetrance is complete.

7. Lines of action

There are two broad methods by which one could overcome genetic defects; elimination of the defective from the population or reduction of the defective gene frequency by selection and planned mating. The first is difficult to achieve and depends on the types of genes involved and the second method could therefore be considered a reasonable approach.

The action to be taken if a lethal or semi - lethal genetic abnormality is discovered in a herd would depend on the type of herd, and the seriousness of the abnormality.[69] The remedial measures practised in a commercial herd may be somewhat different from those practised in breeding a herd. However, two methods are available to a breeder to reduce the frequency of the genetic defect, namely, selection (culling) and breeding (plan mating).

(*a*) All males and females that have ever produced offspring with lesions characteristic of the genetic abnormality under study must be culled.

(*b*) Replace sires and dams with animals that have either had no history of the defect in their pedigrees or minimal probabilities of being a carrier.

(*c*) Cull all animals that are closely related to the defective offspring even if they are normal, until they are proven clean.

(*d*) Avoid the over use of a particular herd sire especially if he is not fully progeny tested.

(*e*) Cross breed to reduce the occurrence of a genetic defect that may be common to a particular breed group.

8. Conclusions

The present paper discusses some aspects related to the genetics of inherited abnormalities. The first question one should ask when an abnormality appears in a herd is whether it is environmental or hereditary. A hereditary basis is best indicated if the abnormality is confined to certain breeding individuals. Hereditary abnormalities often go undetected especially when progeny are born dead and serious consideration must be given to this aspect. Genetic defects are often of a recessive type. Recessive genetic defects are difficult to select against, and selection becomes very ineffective when the defective gene frequency is low. Furthermore, if penetrance of the defective gene is incomplete, selection will be still less effective in reducing gene frequencies.

Heterozygote advantage and incomplete gene penetrance were recognised as two important factors that help to keep defective gene frequencies stationary in populations. Complete elimination of recessive defective genes from a population is virtually impossible especially if penetrance is incomplete. Thus a reduction of gene frequencies must be achieved through a system selection and planned breeding.

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Appendix 1

Partial Listing of Genetic Abnormalities — Cattle, Sheep, Goats and Swine.

Abnormality	Inheritance	Reference/Source
Cattle		
Achondroplasia 1	Lethal-partially dominant requiring two genes to have a lethal effect. Dexter x Kerry Jersey, Hereford & Friesian cattle.	Lasley (1978)
Achondroplasia II	Lethal-Mode of inheritance appears to be recessive Telem ark, Jersey, Guernsey, Ayrshire cattle.	Lasley (1978)
Achondroplasia III	Lethal-recessive Jersey cattle.	Lasley (1978)
Achroteriasis	Single autosomal recessive gene	Geringer (1977)
Adactly	Autosomal and recessive.	Liepold *et al* (1970)
Agnathia	Lethal-Sex linked recessive, Angus and Jersey Cattle.	Lasley (1979)
Amputated	Lethal-recessive and autosomal Swedish Friesians.	Lasley (1978)
Arthrogryposis	Lethal-autosomal recessive, incomplete penetrance-Charolais cattle.	Berg *et al* (1974)
Brachygnathia	Non lethal-recessive gene probable.	Dunn *et al* (1972)
Bull dog head	Non lethal-recessive Jersey cattle.	Lasley (1978)
Cerebral hernia	Lethal-probably recessive, Holsteins.	Lasley (1978)
Cerebrospinal fluid pressure increase	Probably recessive.	Fransen *et al* (1958)
Comprest condition	Lethal partially dominant.	Lasley (1978)
Congenital atazia	Autosomal and recessive.	Johnston *et al* (1958)
Congenital cataract	Non lethal-recessive Hereford.	Gregory *et al* (1943)
Congenital debility	Condition transmitted probably genetic, Brown swiss cattle.	Derlogea *et al* (1958)
Congenital head abnor-- malities and Brachynathia	Autosomal dominant.	Ernest *et el* (1977)
Congenital ichthyosis	Inherited as a lethal factor, Zebu cattle.	Verjacko *et al* (1974)
Congenital lethal Spasms.	Lethal-recessive.	Gregory *et al* (1944)
Congenital porphyria	Non lethal-simple recessive.	Madden *et al* (1958)
Corkscrew claws	Probably genetic.	Bouckaert *et al* (1958)

Abnormality	Inheritance	Reference Source
Culard (double muscling)	One pair of modified genes with a wide range of activity.	Hanset (1972), Kidwell *et al* (1952)
Curved limbs	Lethal-recessive Guernsey.	Freeman (1958)
Dermatosparaxis	Lethal-recessive mode of inheritance.	Hanset *et al* (1974)
Doddler cattle	Lethal-monofactorial autosomal recessive.	High *et al* (1958)
Duck legged cattle	Non lethal-autosomal dominant.	Lasley (1978)
Dwarfis. achondroplastic	Probably recessive.	Tyler *et al* (1959).
Epilepsy	Dominant.	Lasley (1978)
Epitheliogenesis imperfecta.	Inheritance as a single autosomal recessive.	Liepold *et al* (1973)
Flexed pasterns	Semi lethal-autosomal recessive Jersey cattle	Lasley (1978)
Hairlessness	Recessive gene-reported in many breeds.	Lasley (1978)
Harelip	Not well understood epistasis may be involved, Shorthorn.	Lasley (1978)
Hydrocephaly	Lethal-recessive, reported in several breeds.	Lasley (1978)
Hypoplasia of ovary	Non lethal-recessive gene with reduced penetrance.	Lasley (1978)
Impacted molars	Lethal recessive in Shorthorn cattle.	Lasley (1978)
Limber legs	Semi lethal-autosomal recessive.	Lamb *et al* (1976)
Long headed dwarf	Non lethal-recessive Angus and Hereford cattle.	Lasley (1978)
Micrencephaly	A genetic basis suggested Hereford cattle.	Fielden (1959)
Mummified foetuses	Lethal-sex linked recessive.	Deaton *et al* (1959)
Muscle contracture	Lethal-recessive.	Lasley (1978)
Muscle contracture and chondrodysplasia syndrome.	Lethal suggested that it is due to a dominant gene with incomplete penetrance	Johanston et al (1958)c
Neuraxial oedema	Lethal-autosomal recessive inheritance.	Weaver (1974)
Occular colombomata	Dominant mode of inheritance Charolais.	Barnett *et al* (1972)
Osteopetrosis	Inherited as an autosomal recessive, Angus cattle.	Huston *et al* (1971)
Polydactylism	Non lethal-probably an autosomal dominant.	Lasley (1978)

Abnormality	Inheritance	Reference/Source
Prolonged gestation	Lethal-recessive	Lasley (1978)
Screwtail	Non lethal recessive	Lasley (1978)
Short spine	Lethal-recessive.	Lasley (1978)
Shorter dwarfism	Semi lethal-recessive.	Johnston *et al* (1950)
Spastic paresis and crooked fore legs	Pentahybrid inheritance with complementary gene action.	Gehrke (1969)
Spinal bifida	Lethal-dominant gene low penetrance.	Nes (1959)
Stumpy	Non lethal-recessive.	Lasley (1978)
Umbelical hernia	Limited to males dominant, Friesian cattle.	Lasley (1978)
Upright pastern	Recessive multifactorial gene effect.	Harmori (1959)
White heifer disease	Sex linked, recessive Shorthorn cattle.	Lasley (1978)
Wry tail	Non lethal-recessive, many breeds.	Lasley (1978)
Xanthosis	Simple recessive.	Hayward *et al* (1978)
Sheep/Goats		
Amputated	Mode of inheritance not well established.	Lasley (1978)
Blindness	Homozygosity for a single recessive factor.	Zwiep (1958)
Congenital (goat) Afibrinogenemia	Mode of inheritance is incompletely dominant.	Breukink *et al*, (1972)
Dwarfism	Semi lethal, recessive	Lasley (1978)
Muscle contracture	Lethal-recessive.	Lasley (1978)
Taillessness	Apparently inherited as a dominant with incomplete penetrance.	Carter (1976)
Swine		
Atresia ani	Lethal-two pairs of dominant genes involved (epistasis); other modes of inheritance and environment may be involved.	Lasley (1978)
Brain hernia	Semilethal-recessive.	Widmaier (1959)
Congenital porphyria	Inheritance due to dominant gene.	With *et al* (1959)
Cranium bifidum	Simple recessive, incomplete penetrance, 2 pairs of genes may be involved	Stewart *et al* (1972)
Crypt ochidism	Sexlimited, recessive.	Johnston *et al* (1958)[a]

Abnormality	Inheritance	Reference Source
Epitheliogenesis imperfecta	Semi lethal-single autosomal recessive gene	Fischer (1958)
Hair Whorls	Non lethal-two pairs of dominant genes (epistasis)	Lasley (1978)
Haemophilis	Semilethal-recessive pol and China breed.	Lasley (1978)
Hydrocephalus	Lethal-recessive.	Lasley (1978)
Mule foot	Non lethal-dominant	Lasley (1978)
Paralysis	Lethal-recessive.	Lasley (1978)
Rhinitis	Simple dominant, inheritance	Koch *et al* (1958)
Splayleg	Dominant, Sex linked.	Lax (1971)
Tongue abnormalities cleft palate and harelip	Autosomal recessive	Nes (1958)
Unbifurcated hooves	Semilethal-dominant.	Gligor *et al* (1959)

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