Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

,

7

A STUDY OF SOME ASPECTS OF GROWTH AND

ł

REPRODUCTION IN TWO INBRED LINES

OF MICE AND THEIR CROSSES

A thesis presented in partial fulfilment of the requirements for the Degree of Master of Agricultural Science in Massey University of Manawatu

BY

24193

R.A.S. LAWSON

Massey University of Manawatu

November, 1964

PREFACE

The mating of closely related individuals is generally believed to result in inferior offspring. Recognition of this danger has been suggested as the reason for evolution of human social customs. However, historical researches suggest that inbreeding unavoidably occurred in small, isolated, ancient communities, and marriage of close relatives was encouraged in the Egyptian, Greek and Hebrew civilisations (Zirkle, 1952).

Inbreeding is likely to have occurred in the isolated flocks of nomads, but it is probable that inbreeding depression, as such, was not recognised until the eighteenth century when the early livestock improvers are reputed to have found that the fertility of their animals deteriorated with continued inbreeding.

Hybrid vigour from cross breeding plants was described by Koelreuter (1766) and confirmed by later botanists. After much detailed work, Darwin (1876) concluded:

"... cross fertilisation is generally beneficial and self fertilisation injurious." and that

- (a) Mechanisms exist widely for the avoidance of inbreeding.
- (b) Inbreeding has effects likely to incur selective disadvantages.

No suitable hypothesis could account for the usually deleterious effects of inbreeding, or the reverse phenomenon of hybrid vigour until the rediscovery of Mendel's work in 1900. The effects of inbreeding can now be explained in terms of the dominance and recessiveness of genes. (Falconer, 1960).

The aim of experiments reported in this thesis was to study growth, reproduction and mortality in two inbred lines of mice, derived from common ancestors, to find if differences between tham had arisen during inbreeding. Reciprocal crosses and matings of the  $F_1$  progeny of these crosses were made to find if hybridisation of the parent lines led to improvements of these characteristics.

This study was suggested by Drs. D.S. Flux, M.F. McDonald and R.E. Munford to whom the author is indebted for advice and guidance.

The author also wishes to acknowledge the assistance of Mr. E. Ormsby in histological preparations, of Mr. P.S. Dale in photomicrography, and of Mr. C. Muir who drew some of the figures reproduced in this thesis. Thanks are also due to the staff of the University Library for their efforts in obtaining literature.

OLIADOR	Ð					
I	CHAPTER I REVIEW OF LITERATURE					
	A. THE IMPORTANCE OF INBREEDING AND INBRED ANIMALS	1				
	I Laboratory Animals	1				
	II Domestic Animals	2				
	B. OBSERVED EFFECTS OF INBREEDING	3				
	I Domestic Animals	3				
	<ul> <li>(a) Occurrence of Abnormalities</li> <li>(b) Mortality, Growth Rate and Feed Economy</li> <li>(c) Reproduction</li> <li>(d) Lactation</li> </ul>	3 4 5 8				
	II Laboratory Animals	9				
	<ul><li>(a) Growth and Nortality</li><li>(b) Reproduction</li></ul>	9 10				
	C. CONCLUSIONS FROM REVIEW OF LITERATURE	12				
II	MATERIALS AND METHODS	14				
	Animals	14.				
	Housing	14				
	Diet	15				
	Breeding Procedures	15				
	Observation and Recording	16				
	Assessment of Prenatal Losses	17				
	Histological Procedure	18				
	Statistical Methods and Presentation of Results	19				
Ĩī	RESULTS	20				
	Age and Weight at Puberty	20				
	Readiness to Mate Following Puberty	21				
	Conception Rates	22				
	Length of Gestation	24				
	Weight Changes of Dams During First Gestation	25				
	Weight of Conceptus	26				
	Litter Size and Mortality	27				
	Growth of Litters from Birth to Weaning	29				

# PAGE

CHAPTER		
III	Mature Weight of Females	31
	Ovum Recovery	32
	Ovulation Rates and Losses During Gestation	33
	Histological Examination of Reproductive Organs	35
	Disease Incidence	37
IV	DISCUSSION	38
	Litter Size and Pup Weight at Birth	38
	Mortality	42
	Growth From Birth to Weaning and Lactational Performance	43
	Growth and Development of Females from Weaning to Maturity	44
	Gestation Length	47
	The Extent and Possible Causes of Infertility and Pre-natal Losses	47
	Disease Incidence	50
´ v	SUMMARY AND CONCLUSIONS	51
REFEREN	CES	55
APPENDI	x	69

•

PAGE

# ERRATA

- p.viii Fig. 8 Should read Prenatal mortality during - . Fig. 13 Should read - Fully developed corpora lutes as found - - -
- p. iz Fig. 15 Should be - - three days post coitum - -
- p. 3 Line 17 no comma following inbreeding.Line 20 transfer not transfers
- p. 6 Line 27 Should read - length occurred because of the absence - -
- p. 8 Line 22 Should read - in the British Guernsey and Frieslan breeds
- p. 14 Line 8 heterozygotes
- p. 15 Line 19 <u>Hymenolepis</u> nana
- p. 16 Line 31 Should read - without them being observed - -
  - Fig. 16 Should read - The typical microscopic appearance of testes - -
- p. 46 Line 11 no comma after puberty
- p. 53 Line 13 Hybridization
- p. 69 Line 3 (CIN o?)

,

TABLE		
I	The effect on a one percent increase in inbreeding coefficient on production by dairy cows.	8
II	Weight (gms) of females at puberty as shown by vaginal opening in inbred (77; 44) and outbred (44x77; 77x44) strains of mice.	20
III	Age (days) of females at puberty as shown by vaginal opening in inbred (77; 44) and outbred ( $\overline{44x77}$ ; $\overline{77x44}$ ) strains of mice.	20
IV	Age (days) of females at puberty as shown by vaginal opening in inbred (77; 44) and outbred (44x77; 77x44) strains of mice. Original data transformed by taking logarithms (following	) 20
V	Mean interval (days) between puberty and observation of a vaginal plug indicating first copulation in each mating system. Females were paired with a mature male on the day of puberty.	21
VI	Conception rate as shown by the number of full term pregnancies resulting from the first observed mating of females in each mating system.	22
VII	Mean number of pups suckled in the first litter by females which became pregnant <u>post partum</u> , and by females which failed to become pregnant <u>post partum</u> .	23
VIII	Lengths of first gestations (days) uncorrected for differences between lines in litter size.	
IX	Lengths of second gestations (days) where full twentyone day lactations were concurrent.	24
X	Mean weight (gms) at the end of first gestation of females in each mating system which conceived at first mating, and the means of these weights transformed by taking logarithms.	25
XI	Mean weights (gms) at conception of females which conceived at first mating in each mating system.	25
XII	Mean weight gain or loss (gms) from conception to completion of first parturition in females of each line which conceived	_,
	at first mating.	25

(vii)

TABLE		FACING PAGE
XIII	Mean weight <u>post partum</u> (gms) of females which conceived at first mating in each mating system.	25
VIX	Mean weights (gms) of first and second conceptuses, as sho by the weight lost by females at parturition, in each mating system; and the pooled mean conceptus weights, over two litters, for each combination of inbred or outbred dam with inbred or outbred litters.	יאיז 26
XV	Mean numbers of pups (including stillbirths) at birth in first and second litters in each mating system; and the pooled mean litter sizes, over two litters, for each combination of inbred or outbred dam with inbred or outbred litters.	27
XVI	Mortality of pups from birth to weaning. (fo	olloving) 27
XVII	The ratio of stillbirths: total births (live births plus stillbirths) as affected by dams of different inbred lines, inbreeding status of dams bearing outbred litters, and inbreeding status of litters born to inbred dams.	27 (following)
XVIII	The effect of dams from different inbred lines, inbreeding status of litters, and inbreeding status of dams on the survival of pups from birth to weaning.	28
XIX	Mean of average pup weight (gms) per dam and litter weights (gms) corrected for litter size in each mating system at birth, 12 days and weaning for first and second litters.	29
XX	Mean mature weights (gms) of females in each mating system at second parturition.	31
XXI	Mean numbers of ova shed at ovulation by inbred and outbred females.	1 33
XXII	Mean numbers of ova shed and number of implantation sites observed on the twelfth day of gestation in each mating system. (fo	ollowing) 33

.

FIGURE

1.	Weight increases during first gestation of females in	
	lines 77, 44, and $F_1$ matings.	25
2.	The components of the mean body weight of pregnant	
	females in each mating system on the last day of	
	first gestation.	25
3.	The growth curves from birth to weaning of inbred pups	70
	in the first and second litters in lines 77 and 44.	30
4.	The growth curves from birth to weaning of outbred pups in first and second litters from the reciprocal crosses	
	of lines 77 and 44.	30
5.	The growth curves from birth to weaning of outbred pups in	
	first and second litters from F <sub>1</sub> matings.	30
6.	The mean growth curves (two litters) from birth to weaning of	
	inbred pups nursed by 77 and 144 dams, outbred pups nursed	
	by 77 and 44 dams (44x77; 77x44) and outbred pups nursed by outbred dams $(F_1)$ .	30
7.	Regression of the number of ova recovered after flushing the	5-
2 •	uterus $3\frac{1}{2}$ days post coitum on the number of ova shed, as	
	shown by the number of corpora lutea in albino mice. (facing)	32
8.	Prenatal_at mortality during first gestation in 77x77	
	matings.	34
9.	Prenatal mortality during first gestation in 44x44 matings.	34
10.	Prenatal mortality during first gestation in 44x77 matings.	34
11.	Prenatal mortality during first gestation in 77x44 matings.	34
12.	Prenatal mortality during first gestation in F, matings	
	$(77x44,^2; 44x77^2)$ .	34
13.	Fully developed corpora lutea is found in the ovaries of 77	- 1
	and F. females three days post coitum.	36
14.	Poor luteal growth with a large blood clot evident in the	36
	ovary of a line 44 female three days post coitum.	50

# FOLLOWING PAGE

FIGURE		
15.	The ovary of a line 44 female three days post coitum	
	showing an unovulated follicle with luteal tissue	
	developing about the periphery.	36
16.	The typical appearance of testes of fertile 77, 44 and $F_1$	
	males showing active spermatogenesis.	36
17.	Testes tissue from a sterile line 44 male showing shrunken	
	seminiferous tubules and no evidence of spermatozoa.	36

#### CHAPTER I

REVIEW OF LITERATURE

# A. THE IMPORTANCE OF INBREEDING AND INBRED ANIMALS:

#### I. Laboratory Animals

As well as being used in genetic studies, highly inbred lines of laboratory animals are used for assays of pharmacological substances, physiological experiments, and nutritional trials. These animals, which theoretically closely approach a homozygous state, are considered to provide genetically uniform biological material which increases the efficiency of such experiments.

Recent work has indicated that meny inbred sub-lines derived from originally highly inbred lines, have diverged from one another with respect to some morphological characteristics (Grünneberg, 1954; NoLaren and Michie, 1954; Deol, Grünneberg, Searle and Truslove, 1957; Carpenter, Grünneberg and Russel, 1957; Bailey, 1957).

This divergence is probably a result of the occurrence and rapid fixation of mutations in inbred sublines rather than residual segregation (McLaren and Michie, 1954).

Comparisons of inbred and outbred animals have indicated that the heterozygote seems more stable to environmental influences (Lerner, 1954). Robertson and Reeve (1952) suggest that this is because of greater "biochemical versatility" in the heterozygote which enables it to buffer itself against environmental changes.

Because the uniformity of inbred lines is suspect, and because of lowered variability in heterozygous animals it has been suggested that  $F_1$  animals, resulting from the crossing of highly inbred lines, may be more suited to many types of experiment (Grünneberg, 1954; Biggers and Claringbold, 1954; Biggers, McLaren and Michie, 1958). Such animals combine lowered variability with genetic uniformity. There is the possibility that further experimentation with crosses of various inbred lines may produce  $F_1$  animals peculiarly suited to different types of experiment.

Regardless of whether inbred or hybrid animals prove to be more suitable, the practice of inbreeding is necessary to provide genetically uniform experimental animals of both types.

# II. Domestic Animals

Because it increases honogyosity and allows the elimination of unwanted genetic material while allowing desired characteristics to be fixed inbreeding, allied with careful selection, is used to develop breeds and strains of livestock with particular inherited characteristics. Such methods were reputedly used in the eighteenth and nineteenth centuries to establish the breed types which are the ancestors of modern sheep and cattle breeds.

The development of the Santa Gertrudis beef breed is a recent example of the use of inbreeding to establish a new breed with particular inherited characteristics (Rhoad, 1949, 1955).

When the numbers of livestock in a country, such as New Zealand, are considered in relation to the numbers originally imported, and the grading up processes involved in changing from a predominantly multipurpose national herd to specialised beef and dairy breeds it is apparent that inbreeding has occurred (Stewart, 1952, 1954).

Likewise pure-breeding and line-breeding systems, as employed by breeders to protect a family thought to have particular merit from contamination by grade stock, or to preserve the genetic material of an admired ancestor, lead to mild, but unwanted inbreeding (Lush, 1948; Stewart, 1954).

Inbreeding can also be used to uncover undesirable recessive characteristics (King, 1955). It is doubtful if losses of this type are of importance relative to the cost and time involved in testing. Such testing may be desirable where animals are to be widely used, as in artificial breeding, since wide dispersal of undesirable recessive genes could occur. The effects of these genes could become apparent when semen from the same, or a related sire, is used on progeny of the original carrier.

In view of the wide occurrence of inbreeding in animal husbandry, as well as the probability of quicker rises in inbreeding levels with intensive artificial breeding, knowledge of the effects of inbreeding on growth conformation, production and reproduction is important (Dickerson, 1940).

Inbred lines of domestic animals have been established in attempts to produce "hybrid vigour" in animals by crossing selected inbred lines. Advances in this field are slow and costly because of the long generation intervals and low reproductive rates of livestock. In addition characteristics associated with reproductive performance, as well as being most susceptable to hybrid vigour, have low heritabilities and are severely affected by inbreeding depression (Rae, 1953; Sang, 1956).

Since many inbred lines become extinct during inbreeding, and in order to increase the probability of superior lines occurring, it is necessary to set up numerous inbreeding lines. Surviving lines can them be tested for general and specific combining ability and used to establish hybrid lines (Fisher, 1949; Falconer, 1960).

Systematic studies of the effects of inbreeding and testing of inbred lines for crossing ability have been carried out by the Regional Swine Breeding Laboratory in the United States, and the Agricultural Research Council of Great Britain. The results of these experiments are reviewed by Craft (1943, 1953), Donald (1955), and Fredeen, (1956).

The intensive conditions under which pigs can be managed allows records to be kept with relative ease while their prolificacy and short generation interval makes pigs suitable for this type of work. In other livestock inbreeding, progress is slower, and there is less probability of having progeny of each sex to continue an inbred line. It is possible that the application of superovulation of immature animals (Marden, 1953) and ovum transfers techniques (Averill and Rowson, 1958) could be used to aid the establishment of inbred lines of livestock.

The theoretical effects of inbreeding and genetic mechanisms involved are discussed by Lush (1948), and Fredeen (1956). Mathematical considerations of inbreeding are discussed by Fisher (1949), and Lush (1948) reviews methods used to measure inbreeding.

#### B. OBSERVED EFFECTS OF INERFEDING:

### I. Domestic Anipals

# (a) Occurrence of Abnormalities:

Inbreeding of swine was accompanied by an increase in the occurrence of abnormalities from 4.4 to 9.4 percent (Donald, 1955). Similar increases were observed in the United States work raviewed by Craft (1953).

The incidence of deformed calves in an inbred Guernsey line indicated the presence of a recessive gene (Woodward and Graves, 1935). No such defects occurred in Friesians (Woodward and Graves, 1946), but Rollins, Mead, Regan and Gregory (1949) reported dwarfs in an inbred Jersey line and Thompson, Cranek and Ralston (1957) suspected that lethal recessives were the cause of stillbirths in American Red Danish cattle. In sheep blindness inherited as a partial recessive has been reported (Ragab and Askar, 1954).

(b) Mortality, Growth Rate and Feed Economy:

Growth rate and feed economy were variously affected in different inbred lines of pigs (Craft 1953; Fredeen, 1956). A decline, with increased inbreeding, in litter and individual weights between birth and weaning has been shown by Dickerson, Blunn, Chapman, Knottman, Krider, Warwick and Whatley (1955), and Bradford, Chapman and Grummer (1958). Hodgson (1935) found birth weight to be unaffected by eight generations of brother-sister mating. Winters, Cummings and Stewart (1947) and Fine and Winters (1952) suggest that less rapid inbreeding combined with a flexible system of selection can minimise the deleterious effects of inbreeding so neither inbreeding of the dam, or of her litter, affects growth and survival between birth and weaning.

The birth weight of inbred Holstein cattle (Woodward and Graves, 1946; Dickerson, 1940) and Black Pied cattle (Nowicki, 1963) declined with inbreeding.

Bartlett, Reece and Lepard (1942) suggest that selection can be used to prevent depression of birth weight in cattle if inbreeding coefficients do not exceed .20 and Eartin, Jacobson, EcGilliard and Homeyer, (1962) find inbreeding has little effect on birth weight or growth rate at coefficients below .15.

The growth rate of Holstein cows was depressed by inbreeding (Nawke, Tyler and Casida, 1954; Menge, Mares, Tyler and Casida, (1960). Inbreeding of enimals of beef breeds led to lighter weights for age and poorer growth rates and feed economies (Stonaker, 1954; Burgess, Landblom and Stonaker, 1954; Swiger, Gregory, Koch and Arthaud, 1961; Alexander and Bogart, 1961; Brinks, Clark and Kieffer, 1963).

At maturity inbred Friesians were lighter than outbreds, but differences were less marked than at birth, (Woodward and Graves, 1946). The inbreds had a higher mortality and were conspicuously less active as mature cows.

Body weight, growth rate, withers height, and heart girth of mature animals were depressed in inbred Holstein and Jersey cows (Baker, Mead and Regan, 1945; Rollins, <u>et al.</u>, 1949). As inbreeding progressed Jerseys were more affected than Holsteins. Swett, Matthews and Fohrman, (1949) found an increase of inbreeding coefficient to .646 decreased body weight, but only slightly affected skeletal size of Holstein cows. Organ weights were variously affected. There was a tendancy for endocrine glands to be reduced in size with inbreeding although thyroid weight increased. No general effect was noted on the variability of the factors studied.

After a series of trials it was concluded that, if genetically superior foundation stock are used, and intensive selection practiced, weight and size of Holstein cows could be maintained provided inbreeding coefficients did not exceed .20 (Bartlett, <u>et al.</u>, 1942; Bartlett and Margolin, 1944; Margolin and Bartlett, 1945).

Levels of inbreeding ranging from 0 to .4 (average 0.1) in weaning, yearling and mature ewes and rams of the Rambouillet, Colombia, Corriedale, and Targhee breeds indicated that inbreeding in sheep had its most detrimental effects on mutton characteristics - body weight, type and condition (Hazel and Terrill, 1945a, b; 1946; Terrill, Sidwell and Hazel, 1947, 1948a, b.)

A similar depression of body weight, growth rate and survival, was noted in inbred Merino sheep (Morley, 1954; Doney, 1957, 1958), and birth and weaning weights of singly born lambs were lower in inbred Ossimi sheep (Ragab and Askar, 1954). Greater mortality occurred in inbred lambs than in outbreds between birth and weaning (Glembockii, 1957; USDA, 1952).

Doney (1959) found that administration of pituitary extract to inbred, but not to outbred lambs, improved growth rate. He concluded that inbreeding may partly exercise its detrimental effects by depression of pituitary function.

(c) Reproduction:

Inbred pigs have been shown to be slower in maturing than outbred pigs. Thus at puberty, as shown by age at first cestrus, inbred gilts were older than outbred gilts (Foote, Waldorf, Chapman and Self, 1956; Squiers, Hauser, Dickerson and Mayer, 1949; Warnick, Wiggins, Casida, Grunner, 1951), and inbred gilts were older at first farrowing (Donald, 1955).

Over two years five inbred strains of gilts maintained their characteristic weights, and ages at puberty. Although within lines weight at ages between birth and puberty was significantly negatively correlated with age at puberty, lines which tended to be heaviest at 154 days were slower to reach puberty. (Warnick et al., 1951). They suggest that inbreeding with selection for growth rate has led to lines with characteristic ages and weights at puberty, and that lines genetically superior for growth are retarded in rate of sexual maturation.

A similar negative correlation between growth rate and age at puberty has been noted by Constock and Winters (1944).

Such a relationship of growth to rate of maturation was not found in boars (Wiggins, Warnick, Grunner, Casida and Chapman, 1951). They found that lines of inbred boars differed in age and weight at puberty as shown by willingness to mate. Age at puberty was negatively correlated with weight at earlier ages and positively correlated with growth rate. Sperm was present in the testes of animals of these lines before they showed willingness to mate.

The growth of testes, development of the seminiferous tubules and the onset of stages of spermatogenesis were slower in inbred lines of boars (Green and Winters, 1945a; Andrews and Warwick, 1949; Hauser, Dickerson and Mayer, 1954). Differences in the age at onset of sexual behaviour and the extent to which it was displayed could be related to differences between lines in 17ketosteroid excretion. (Green, Winters, Rash and Dailey, 1942; Green and Winters, 1945b). These differences between lines in 17-ketosteroid excretion probably reflect differences in the levels of male steroid production.

Hodgson (1935) reported a reluctance of inbred animals to mate.

A delay in the attainment of puberty associated with slower growth has been found in Holstein cows. (Hawke, <u>et al.</u>, 1954; Menge, <u>et al.</u>, 1960).

Longer cestrous cycles were found in inbred sheep (Hulet, Blackwell, Ercanbrack, Price and Wilson, 1962). The daughters of inbred cows had longer cestrous cycles than the daughters of outbred cows, while inbreeding of the daughters themselves, only slightly affected cestrous cycle length. This change in mean cycle length was due to the absence of short cycles. No reason is apparent for this maternal effect (Mares, Menge, Tyler and Caside, 1961a).

A decline in reproductive success with inbreeding in livestock has been generally observed.

From an analysis of Berkshire pedigrees Hughes (1933) concluded that an inbreeding coefficient of .74 had been reached. Inbred pedigree pigs had larger litter sizes than random bred pigs. No indication as to the extent of selection in these two herds is given. McPhoe, Russel and Zeller (1931) reported a decline in pig fertility and vigour with inbreeding, while Hodgson (1935) found no effect on litter size.

More recent work, reviewed by Graft (1953) and Donald (1955), has revealed a decline in litter size, vigour at birth, and a poorer survival rate in inbred pigs. This decline in litter size averaged one third of a pig at farrowing and half a pig at weaning per ten percent increase in inbreeding. Similar results are shown by other workers (Dickerson, <u>et al.</u>, 1955; Bradford, <u>et al.</u>, 1958; Rognoni and Brambilla, 1958).

The observed reduction in litter size was attributable to both inbreeding of the sow and of her litter (Dickerson, et al., 1955; Bradford, et al., 1958).

The number of services per conception was more in inbred dairy cattle (Woodward and Graves, 1946). Inbred beef cattle raised fewer calves than outbreds (Stonaker, 1954), and barren Hereford and Aberdeen Angus cows and their presumed conceptuses had higher inbreeding coefficients than did pregnant cows (Bovard and Priode, 1963).

Inbred sheep suffered more abortions, had lower lambing percentages and were older when they reached maximum reproductive performance than were random bred sheep (Morley, 1954; Glembockii, 1957; Doney, 1957, 1958).

Heritable recessive defects in sperm morphology leading to complete infertility in bulls have been reported (Donald and Hancock, 1953; Gregory, Mead, Regan and Rollins, 1951). It has been suggested that an increase in sperm abnormalities and a general decline in semen quality observed in inbred bulls could be partly due to a deterioration in the environment for sperm maturation with inbreeding. (Harris, Faulkner and Stonaker, 1960; Sostak, 1961).

Except in cases of complete sterility, which occurred more often in inbred pigs (Donald, 1955), once they reached puberty inbred boars were no less fertile than outbred boars (Wiggins, <u>et al.</u>, 1951; Hauser, <u>et al.</u>, 1954). There was no difference between inbred and outbred lines in the proportion of ova fertilised (Squiers, Dickerson, and Mayer, 1954).

Evidence for differences in ovulation rate between inbred and oubred animals is inconclusive. Inbred lines of gilts had characteristic ovulation rates, but inbreds did not have poorer ovulation rates than outbreds, (Squiers, Hauser, Dickerson and Mayer, 1949). Inbred sows in this trial tended to have poorer ovulation rates, but few were examined. In another study (Squiers, <u>et al.</u>, 1954) ovulation rate in gilts was depressed by .55 ova per ten percent of inbreeding.

Since evidence for poorer fertilisation rates and, or lower ovulation rates in inbred animals is not conclusive post fertilisation losses could be a cause of lower reproductive performance. Such losses could be due to the segregation of lethal genes and to poorer viability of inbred embryos associated with a deteriorated uterine environment in inbred dams.

# TABLE I:

# The effect of a one percent increase in inbreeding coefficient on production by dairy cows

	level of abreedin		Fat Yield lbs	Fat Z	Source
Holstein-Friesian	•37	- 74	-2.3	-	Tyler, <u>et.el</u> ., 1949.
Holstein-Friesian	<b>₅</b> 50∻	- 30 (Approx)	-1.9	-0.007	Woodward and Graves, 1946.
Holstein	•44	-209.8	-4•9	+0,008	Laben, <u>et.al</u> ., 1955.
Holstein-Friesian	Mild	- 66	-2.0	+0 <sub>°</sub> 003	Laben and Herman, 1950.
Friesian	**	-	-4-5	-	Nelson and Lush, 1950.
Friesian	-	<del>~</del> 30.0	<del></del>	0.0	Robertson, 1954.
Holstein	•34	- 54	-1.74	+0.003	Krosigk and Lush, 1959.
American Red Danish Cattle	æ	- 23.1	<u>-0.3</u>	<b></b>	Thompson, <u>et.al</u> ., 1957.

.

-

Pomeroy (1952) concluded that early embryonic death and resorption was the most likely cause of lowered fertility in inbred pigs.

A decline of .80 embryos per ten percent inbreeding in pigs examined at 25 days was found by Squiers, <u>et al</u>., (1954). Vernon, <u>et al</u>., (1952) found still births increased by 1.6 percent per ten percent increase in inbreeding of the dam.

In cows, inbreeding of a potential calf resulted in a poorer fertilisation rate or more early embryonic losses; inbreeding of the dam promoted more later embryonic losses, particularly in mature cows. (Mares, <u>et al.</u>, 1961b). Losses up to 150 days of gestation were greater in inbred cows (Hawke, <u>et al.</u>, 1955).

Some evidence for an increase in gestation length in inbred pigs is cited by Craft (1953). An association between inbreeding of a cow, but not of her calf and gestation length was reported by Rollins, Laben and Mead (1956). Other factors may have been confounded with the effect of inbreeding on gestation length reported here. Foote, Tyler and Casida (1959) could show no effect of inbreeding or gestation length in Jersey cows.

(d) Lactation:

Early workers, relying on analysis of pedigrees, were unable to demonstrate any clear effect of inbreeding on production by dairy cows. Joyce (1931) concluded that inbreeding, as calculated from pedigrees, did not affect Ayrshire production ; and Asdell (1945) concluded that the top producing 100 cows in the Guernsey and Friesian breeds were no more or less inbred than the breed average. British Jerseys producing over 10,000 pounds of milk per lactation were less inbred than the national average (Smith and Buchanan, 1928). Clear effects of inbreeding on production are shown when experiments to deliberately inbreed dairy cattle are conducted.

It can be seen in Table 1 that inbreeding is associated with a fall in milk and butterfat yields. The effect on butterfat per centage is variable. A similar effect was reported in a Polish experiment (Nowicki, 1963) but Davis <u>et al.</u>, (1953) report that levels of inbreeding with selection of .41 were reached over 30 years and milk and fat yields were improved.

The increases in fat percentage reported are not surprising since it is widely known that environmental factors which depress milk yield, often have a compensating effect to increase butterfat percentage. Negative genetic correlations between milk yield and fat percentages have also been reported (Robertson, Waite, and White, 1956).

Laben, Cupps, Mead and Regan, (1955) suggest that the effect of inbreeding on production may be curvilinear and serious declines in production may not occur until inbreeding coefficients exceed .20.

Inbreeding of Sardinian sheep led to a decline in milk yield and fat percentage (Dassat, 1950).

#### II. Laboratory Animals

# (a) Growth and Mortality:

It is reported by Lerner (1954) that inbreeding led to an increase from 3.9 to 45.5 percent in the preweaning mortality in rats as the inbreeding coefficient was raised from 0 to .41 in the experiments of Ritzema Bos (1894). Feldman (1926) observed that inbred rats were more susceptible to disease, but other workers have found no loss of vigour in inbred rats (King, 1918-19; Craig and Chapman, 1953). In these experiments selection for vigour was applied.

Inbreeding increased post natal mortality in guinea pigs (Eaton, 1932), and in mice (Chai, 1959).

Feldman (1926) found inbred rats grew less well than outbreds and Craig and Chapman (1953) found that inbred lines had lower body weight at 13 weeks than did outbred rats from the same source. However, King (1918-19) was able to carry out twenty two generations of brother-sister mating, with selection, and produce inbred rats superior in mature size to random bred rats.

The growth rate of Dutch rabbits declined with inbreeding (Microwsky and Mönigs, 1927), but Pease (1928) found inbreeding had no effect on mature weight in Polish rabbits. Ragab, Asker and Madkour (1961) inbred rabbits to an inbreeding coefficient of .33; although birth weights declined weaning weights were improved. In guinea pigs (Wright, 1922; Eaton, 1932) changes were observed in the ranking of five surviving inbred lines over 25 years of inbreeding.

In these experiments five lines of the original 25 inbred lines survived inbreeding, and these were originally above average in their reproductive performance. These experiments seem to show a general decline in litter size, growth rate, and an increase in mortality with inbreeding. The origins of the random bred control, which was begun some years after inbreeding began, are not stated.

Inbreeding affected the lactational performance of mice as measured by litter weight at twelve days (Falconer, 1947). This was partly due to impaired lactation in the inbred dam and partly due to impaired growth rate in the inbred litter. Inbreeding with selection enabled inbred dams to equal outbred dams in lactational performance when suckled by outbred litters.

Pease (1928) found that maternal ability was impaired by inbreeding in rabbits.

(b) Reproduction:

Many inbred lines became extinct through failure to produce enough young to carry on inbreeding (Guinea pigs : Wright, 1922; Rabbits : Microwsky and Königs, 1927; Mice : Bowman and Falconer, 1960).

A decline in litter size with inbreeding has been shown in rats (Ritzema Bos, 1894; Feldman, 1926), rabbits (Pease, 1928), guinea pigs (Eaton, 1932), and in mice (Bowman and Falconer, 1960). King (1918) found that rats, inbred with selection, were superior in fertility to random bred rats after twenty two generations of inbreeding with selection.

Highly inbred rats of the King albino strain grew as well, reached maturity earlier, and had a superior ovulation rythm to hybrids of the Long Evans strain (Evans, 1928). Inbreeding was accompanied by greater variability in time of vaginal opening in mice (Yoon, 1955) and increased the age at which first litters were born (Strong and Fuller, 1958; Strong, 1960).

Loziak(1959) found that cestrous cycles were often prolonged in inbred mice and some stages of the cycle were often missing.

Congenital sterility as well as difficult parturition was considered to be the cause of lowered fertility in rats (Feldman, 1926).

Male sterility characterised by cryptorchidy and abnormal fatness was found in Polish and Flemish rabbits (Pease, 1928). This condition was possibly due to a recessive gene as it was eliminated in Polish rabbits after seven generations of inbreeding.

Krzanowska, (1960a) found inbred male mice had lower fertilisation rates than outbred males.

Less viable sperm was found in ejaculates from inbred rabbits than in cross bred rabbits (Sokolovskaja, 1950), and inherent line and breed differences in morphological and physiological characteristics of sperm from inbred lines of mice and rabbits have been reported (Beatty and Napier, 1960; Beatty and Sharma, 1960; Sharma, 1960). These differences could lead to variations in fertility between lines, although Falconer and Roberts (1960) found inbreeding of the male parent had no effect on fertility.

Impaired sex behaviour in inbred rats resulted in no copulation occurring in 70 per cent of inbred matings compared with 10 per cent in non-inbred matings (Evans, 1928).

No difference in ovulation rate was seen in inbred and outbred mice by Falconer and Roberts (1960) but Krzanowska (1960b) found inbreds produced slightly fewer ova.

Failure of fertilisation and, or greater pre-implantation losses were found to be the cause of smaller litters in inbred mice (Falconer and Roberts, 1960). Post-implantation losses were similar in both inbred and outbred mice.

Greater pre- and post- implantation losses in inbred mice than in outbred mice were observed by Krzanowska (1955, 1960b) and Leziak (1959). The extent to which losses occurred at different stages of gestation was characteristic of different inbred lines (Krzanowska, 1960b).

# C. CONCLUSIONS FROM REVIEW OF LITERATURE

Since inbreeding occurs in both laboratory and domestic animals, knowledge of its effects on variability, growth, reproduction and production of milk and meat is important. Research into the possibilities of crossing selected inbred lines could lead to the development of improved or specialised hybrid strains of animals.

Experiments in which animals have been inbred have indicated that :-

- 1. Inbreeding is often accompanied by increased mortality and reduced reproductive performance, so that many inbred lines become extinct. The extent to which inbreeding depression has its effects varies between inbred lines; lines surviving to high levels of inbreeding often do not have their preformance severely depressed.
- 2. Slow rates of inbreeding with constant selection have sometimes enabled high levels of inbreeding to be reached with accompanied improvements in the performance of the inbred animals. Inbreeding is not incompatible with animal improvement, but selection cannot generally combat the depressive effects of inbreeding if inbreeding coefficients exceed .20.
- 3. It seems generally assumed that the amount by which a character is depressed by inbreeding increases linearly as inbreeding coefficients rise. Some workers suggest this relationship may be curvilinear so that inbreeding effects are not marked at low levels of inbreeding.
- 4. There is some evidence to suggest that the variability of some characteristics is greater within inbred lines than in the  $F_4$  hybrids of inbred lines.
- 5. Probably as a result of the segregation of deleterious recessive genes, an increase in the incidence of abnormalities occurs with inbreeding.
- 6. Inbred animals are often slower to reach puberty than non inbred lines.
- 7. Complete infertility, probably as a result of segregation of recessive genes, has been reported in some inbred male animals. Differing sperm, and semen characteristics have been found in inbred lines and poorer quality semen from inbred animals has been reported.

- 8. A decline in reproductive performance has generally been found to accompany inbreeding. Evidence of lower ovulation rates is inconclusive; apparently depressed performance results from increases in embryonic deaths caused by lethal recessives and, or poorer viability of inbred embryos associated with a deteriorated uterine environment in inbred females.
- 9. Post-natal mortality is generally greater in inbred than in outbred animals.
- 10. Inbred animals at birth are often lighter than outbred animals and grow less rapidly.
- 11. Owing to slower growth, and lighter mature weights meat production by inbred livestock is poorer than in outbred animals. Milk production declines with inbreeding in cows and sheep. Poorer milk production by inbred laboratory animals may partly eccount for the slower growth of their litters.
- 12. The poorer performance of inbred animals is possibly associated with an imbalance of the endocrine system.