

UNIVERSITY OF MISSOURI

COLLEGE OF AGRICULTURE

AGRICULTURAL EXPERIMENT STATION

RESEARCH BULLETIN 105

# GROWTH AND DEVELOPMENT

*With Special Reference to Domestic Animals*

- X. The Relation Between the Course of Growth and the Course of Senescence with Special Reference to Age Changes in Milk Secretion.

(Publication authorized June 1, 1927)



COLUMBIA, MISSOURI

JUNE, 1927

# Agricultural Experiment Station

**EXECUTIVE BOARD OF CURATORS.**—F. M. McDAVID, Springfield; MERCER ARNOLD, Joplin; H. J. BLANTON, Paris.

**ADVISORY COUNCIL.**—THE MISSOURI STATE BOARD OF AGRICULTURE

**STATION STAFF, AS OF JUNE, 1927**

STRATTON DULUTH BROOKS, A.M., LL.D., President

F. B. MUMFORD, M.S., D. Agr., Director      S. B. SHIRKY, A.M., Asst. to Director  
MISS ELLA FAHMEIER, Secretary

## AGRICULTURAL CHEMISTRY

A. G. HOGAN, Ph. D.  
L. D. HAIGH, Ph. D.  
W. S. RITCHIE, Ph. D.  
A. R. HALL, B. S. in Agr.  
J. E. HUNTER, A.M.  
C. L. SHREWSBURY, A. B.  
E. W. COWAN, A. M.  
ROBERT BOUCHER, A. B.

## AGRICULTURAL ECONOMICS

O. R. JOHNSON, A. M.  
S. D. GROMER, A. M.  
BEN H. FRAME, A. M.  
F. L. THOMSEN, Ph. D.  
G. B. THORNE, B. S. in Agr.

## AGRICULTURAL ENGINEERING

J. C. WOOLEY, M. S.  
MACK M. JONES, B. S. †  
R. R. PARKS, B. S. in Agr. Eng.  
HARRY MILLER, B. S. in Agr. Eng.

## ANIMAL HUSBANDRY

E. A. TROWBRIDGE, B. S. in Agr.  
L. A. WEAVER, B. S. in Agr.  
A. G. HOGAN, Ph. D.  
F. B. MUMFORD, M. S.  
D. W. CHITTENDEN, A. M.  
F. F. MCKENZIE, Ph. D.\*  
M. T. FOSTER, B. S.  
M. G. CLARK, M. S.

## BOTANY AND PHYSIOLOGY

W. J. ROBBINS, Ph. D.  
I. T. SCOTT, Ph. D.

## DAIRY HUSBANDRY

A. C. RAGSDALE, B. S. in Agr.  
WM. H. E. REID, A. M.  
SAMUEL BRODY, A. M.  
C. W. TURNER, A. M. †  
C. W. WEBER, B. S. in Agr.  
E. C. ELTING, M. S.  
WARREN GIFFORD, M. S.  
E. R. GARRISON, B. S. in Agr.  
J. S. MATTHEWS, B. S. in Agr.

## ENTOMOLOGY

LEONARD HASEMAN, Ph. D.  
K. C. SULLIVAN, A. M. †  
C. N. DAVIS, B. S. in Agr.

## FIELD CROPS

W. C. ETHERIDGE, Ph. D.  
C. A. HELM, A. M. †  
L. J. STADLER, Ph. D.  
R. T. KIRKPATRICK, B. S. in Agr.  
B. M. KING, A. M.  
B. B. BRANSTETTER, A. M.  
MISS CLARA FUHR, M. S.\*

## HOME ECONOMICS

MISS MABEL CAMPBELL, A. M.  
MISS JESSIE CLINE, A. M., A. B.  
MISS BERTHA K. WHIFFLE, M. S.  
MISS MARGARET C. HESSLER, A. M.  
MISS ZULU WILLIAMS, A. B.  
MISS E. CHARLOTTE ROGERS, A. M.

## HORTICULTURE

T. J. TALBERT, A. M.  
H. D. HOOKER, Ph. D.  
H. G. SWARTWOUT, A. M.  
J. T. QUINN, A. M.  
A. E. MURNEEK, Ph. D.

## POULTRY HUSBANDRY

H. L. KEMPSTER, B. S. in Agr.  
EARL W. HENDERSON, A. M.

## RURAL SOCIOLOGY

E. L. MORGAN, A. M.  
HENRY J. BURT, A. M.  
MISS GLADYS MULLENBERG, A. B.

## SOILS

M. F. MILLER, M. S. A.  
H. H. KRUSEKOFF, A. M.  
W. A. ALBRECHT, Ph. D.  
RICHARD BRADFIELD, Ph. D.  
R. E. UHLAND, A. M.  
F. L. DAVIS, B. S. in Agr.

## VETERINARY SCIENCE

J. W. CONNAWAY, D. V. M., M. D.  
O. S. CRISLER, D. V. M.  
A. J. DURANT, A. M., D. V. M.  
H. G. NEWMAN, A. M.  
ANDREW UREN, D. V. M.

## OTHER OFFICERS

R. B. PRICE, B. L., Treasurer  
LESLIE COWAN, B. S., Secretary  
A. A. JEFFREY, A. B., Agricultural Editor  
J. F. BARHAM, Photographer  
MISS JANE FRODSHAM, Librarian  
E. E. BROWN, Business Manager

\*In service of U. S. Department of Agriculture

†On leave of absence.

## CONTENTS

	Page
Abstract .....	4
Acknowledgments .....	4
I. Introduction .....	5
II. The relation between the course of milk yield and the course of increase in body weight of dairy cattle .....	7
III. Age changes in milk yield during the period of constant body weight .....	17
IV. Changes in the time rate of milk yield with the advance of the period of lactation .....	21
1. Decline in the time rate of milk yield with the ad- vance in the period of lactation .....	21
2. The rise in the time rate of milk yield with the ad- vance of the period of lactation, and the relation between the rising and the declining segment of the lactation curve .....	23
V. Age changes in other physiological processes .....	27
1. Age changes in the time rate of specific mortality.....	27
2. Age changes in the time rate of ovulation in the domestic fowl .....	32
3. The course of healing wounds, and the course of duration of life of fibroblasts <i>in vitro</i> .....	34
4. The course of senescence as inferred from the course of basal metabolism in man .....	35
VI. Summary and conclusion: The relation between growth and senescence .....	39
VII. Appendix .....	47
a. The limit of egg production in the domestic fowl.....	47
b. The limit of milk production in the dairy cow with the advance in the stage of lactation and with ad- vance in age .....	48
c. The relation between the maximum milk production in a lactation period, the relative rate of decline with the advance of the period of lactation, and the total milk production in a lactation period .....	48
d. Equivalence charts between growth in weight and increase in milk yield .....	51
e. The relation between milk yield, butterfat yield, and butterfat percentage in milk .....	57
f. Historical notes relating to the mechanism of milk secretion .....	63

## ABSTRACT

1. During the period of growth in weight, the age changes in milk yield follow the same course as the age changes in body weight; both can be represented by the same equation stated and explained in the text. Some time after the maximum body weight is reached, the milk yield begins to decline. The decline in the time rates of milk yield is exponential. The age curve of milk yield, which is of a rising and declining type, is not symmetrical about its maximum.

2. The time curve of milk secretion with the advance of the period of lactation resembles the age curve of milk secretion, as it is made up of a segment of increasing time rate of milk yield and a segment of decreasing time rate of milk yield and both curves can be represented by the same equation.

3. To substantiate the conclusion, based on age changes in milk yields, that the time rate of senescence increases exponentially with increasing age, the following additional data have been examined for their time relations at different ages: (a) specific mortality in man; (b) ovulation in the domestic fowl; (c) healing of wounds in man; (d) duration of life of fibroblasts *in vitro* in blood serum from chickens of different ages; (e) basal metabolism in man. Taking (a), (b), (c), and (d) as indices of senescence, these data substantiate the conclusion that the degree of senescence increases exponentially with increasing age. The results of the analysis of (e) are inconclusive on account of the inadequacy of comparable data.

4. A discussion is presented concerning the quantitative relation between the course of growth and the course of senescence.

5. The following items are discussed in an appendix: (a) Limiting values for milk production, egg production, etc. (b) The relation between total milk production, maximum production, and the rate of decline in milk production during a lactation period; (c) equivalence charts between growth in weight, and age changes in milk production; (d) the relation between milk yield, butterfat yield, and butterfat percentage; (e) historical notes relating to the mechanism of milk secretion.

## ACKNOWLEDGMENTS

The charts on milk secretion are based on data summarized by A. C. Ragsdale and the writer in the first bulletin of this series (Missouri Res. Bul. 96). While differing in technical details and general outlook, the fundamental ideas on milk secretion presented in this bulletin have their origin in several papers previously published by A. C. Ragsdale, C. W. Turner, and the writer in the *Journal of General Physiology* 1923, Vol. 5, pp. 441 and 777; 1923, Vol. 6, pp. 21 and 31; 1924, Vol. 6, p. 541. It is a pleasure to acknowledge indebtedness to Professor Ragsdale for his encouragement and interest in the preparation of the present bulletin.

A portion of the expenses involved in this investigation was paid from a grant from the Committee on Food and Nutrition of the National Research Council. Grateful acknowledgment is made for this cooperation, which was received through the recommendation of Dr. Graham Lusk, Chairman, and Dr. E. B. Forbes, Chairman of the Sub-Committee on Animal Nutrition. Acknowledgment is made to C. D. Sparrow, H. H. Kibler, R. A. Hase and J. A. Boden, undergraduate students in the University of Missouri, for assistance rendered in the preparation of the charts.

# GROWTH AND DEVELOPMENT

*With Special Reference to Domestic Animals*

## X. The Relation Between the Course of Growth and the Course of Senescence with Special Reference to Age Changes in Milk Secretion

SAMUEL BRODY

### I. INTRODUCTION

Growth is, theoretically considered in a special sense, a reversible process. It is conceivable that a mature animal, when placed under appropriate conditions, will revert to an immature form. As a matter of fact, C. M. Child succeeded in realizing this very transformation in the planarian as indicated diagrammatically in Fig. 1.

But it is not necessary to go to planarians to realize a reversion in the growth process. A dairy cow becomes pregnant, and her mammary glands grow and develop. In the natural course of event, the development reaches a maximum, then it declines; it "grows" old. The cow is bred again and the "youthful" growing condition is restored. This evidently is an example of a reversible process (of course in a special sense).

To take another familiar example: During the lactation period the cow is in a negative balance with respect to calcium and other substances. She loses her substance. At the end of the lactation period when she is "dry" all the losses are regained; an example of a reversible process.

The above cases are, however, special illustrations of the conception of reversibility of the growth process. In general, as far as the organism as a whole is concerned, there is no going back and starting over; and as far as weight and length are concerned, at least for the purpose of quantitative analysis, there is no going forward or backward after approximately one-fourth, or one-third, of the life cycle is passed. A 16-year-old cow—well advanced in years as cows go, and deeply scarred by time—has the approximate size of a 6-year-old animal in her prime of life.

The relatively static nature of body weight and length seriously limits the usefulness of these measurements as indices of age changes in higher organisms. These measurements give a one-sided picture of the developmental process—the side which technically comes under growth only. They have no value whatever as indices of age changes during the very important phase of the life cycle classed under senescence (and occupying two-thirds of the life cycle).

Yet the time relations of senescence have considerable interest not only to the student of general and human biology, but also to the agri-

culturist. In the case of the dairy cow, for example, profitable milk secretion does not usually begin until growth is nearly completed. The major portion of the productive life of the animal occurs not during the period technically classed under growth, when body size is an index of age changes, but during the period which may be classed under senescence.

The same may be said of many other domestic animals, such as the domestic fowl kept for her egg yield, or the working animal kept for its labor.

These considerations suggested the need for as careful an analysis of the time relations of senescence (that is, of the period following consistent growth in weight) as that given to growth in weight and in length. The present bulletin is devoted to this problem.

This bulletin is concerned principally with the age changes in milk secretion in dairy cattle. In order to render the conclusions based on age changes in milk secretion as general as possible, we shall, in addition, examine some other, relatively meager, data on the time relation of senescence.

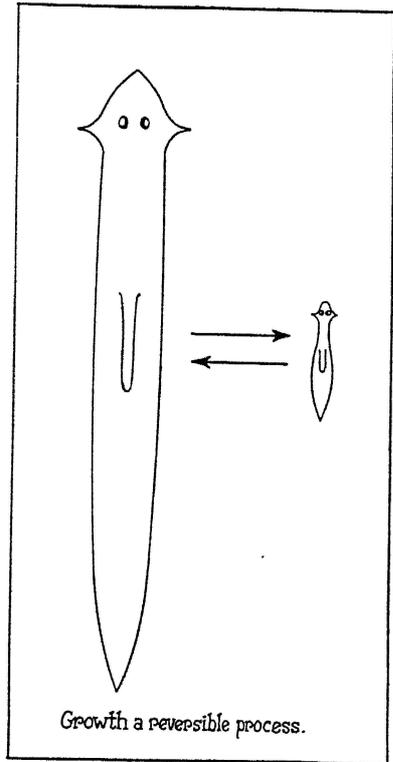


Fig. 1.—While growth is fundamentally a reversible process as indicated by the rejuvenating effect of starvation on planarians it is only theoretically so (or only for certain organs or systems) as far as it relates to higher animals. As far as farm animals are concerned, size (after maturity is reached) is very stationary, being relatively independent of age. (Modified from C. M. Child, 1915.)

## II. THE RELATION BETWEEN THE COURSE OF MILK YIELD AND THE COURSE OF INCREASE IN BODY WEIGHT IN DAIRY CATTLE

The purpose of the present section is to determine whether milk secretion and body weight follow the same course during the period preceding the age of maximum body weight. If we find both to follow the same course, we shall have more confidence in employing the age curve of milk secretion as an index of the course of growth and senescence.

At the outset it may be said that in one sense there is no *a priori* reason for assuming that the milk yield and the body weight should follow the same course during the period of growth, since it is well known that, at least between birth and puberty, the course of development of the reproductive apparatus (with which the mammary glands appear to be intimately related) is not parallel with the course of increase in body weight.

If, however, we contemplate the enormous energy transformations involved in milk production in heavy-milking dairy cows, we are naturally tempted to guess that the body weight (i. e., capacity of the digestive, circulatory, respiratory, excretory systems, etc.) is likely to be the limiting factor in milk production. In other words, given a highly developed (genetic) capacity for milk production, the increase in milk yield and in body weight should follow the same course.

Several simple methods suggest themselves for testing this proposition.

The most obvious method is to plot milk yield against body weight during the period of growth, as in Fig. 2. This figure shows that up to the maximum body weight and maximum milk yield (6 to 8 years), the relation between the two variables is linear; in other words, increasing the body weight by a unit weight (during the period of growth) is accompanied by an increase in milk yield by a unit (a unit of another magnitude) weight.

Another method for demonstrating the same idea, somewhat more complicated but more satisfying from the theoretical point of view, is to fit our usual growth equation to the data on age changes in milk yield. The growth equation referred to is

$$W = A - Be^{-kt} \quad (1a)$$

or

$$W = A(1 - e^{-k(t-t^*)}) \quad (1b)$$

or

$$\frac{W}{A} = 1 - e^{-k(t-t^*)} \quad (1c)$$

in which  $W$  is the milk yield, at the age  $t$ ,  $A$  is the maximum (mature) milk yield,  $k$  is the fractional decline in the increases of the time rates of

milk yield. This equation has been explained in detail in the preceding bulletins of this series where it has been shown to represent the course of growth in weight following the age of puberty.

The fit of equation (1) to the age changes in milk yield would indicate that milk yield and body weight follow the same course, both being expressions (and measures) of the process of growth. It would also indicate that the increases in the time rates of milk yield decrease by a constant relative (or when multiplied by 100 percentage) rate,  $k$ . If for a given group of animals the values of  $k$  are the same for the milk yield

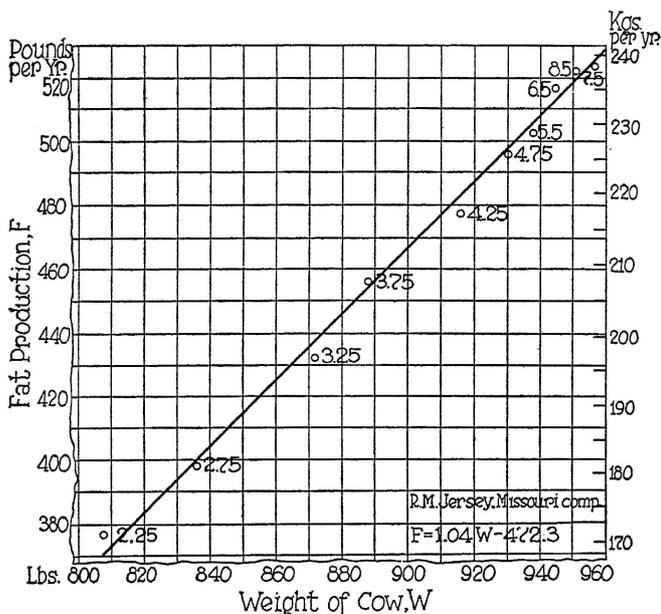


Fig. 2.—The relation between body weight and butterfat yield during the period of growth (2.25 to 8.5 years). The equation indicates that an increase in body weight by one pound is accompanied by an increase in butterfat yield by 1.04 pounds per year. In other words, the mammary function and the body weight follow the same course during this period of the life cycle. (This curve was previously published by Ragsdale, Turner, and the writer in *J. Gen. Physiol.*, 1923, VI, 21.)

data and for the body weight data, then it would mean that both approach the maximum (weight in one case and milk yield in the other case) at the same velocity. If the values of  $k$  and of  $t^*$  are the same for both, then the maximum in both cases is reached at the same age.

It must be emphasized that the same value of  $k$  for two curves does not imply that the two curves are parallel, either on arithmetically coordinate or on arithlog paper. It means that the values of  $A - W$  (see Res. Bul. 97) when plotted on arithlog paper have the same slopes; that

is to say, the rapidities of approach to the mature weights are the same for both curves.

Finally, if equation (1) is found to represent the course of increase in milk yield, then the correspondence between the curves of growth in weight and the curves of milk yield may be further demonstrated by preparing equivalence charts as shown in Fig. 3.

Fig. 4 represents the fit of equation (1) to data obtained on three breeds of cattle which were not on test. These animals, owned by vari-

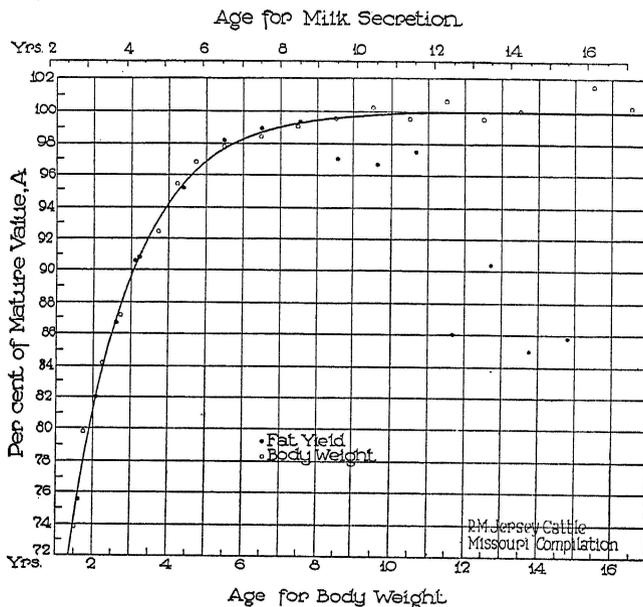


Fig. 3.—Until age of the animal is 8 years, body weight and milk yield follow the same course as demonstrated by the excellent agreement between the age curves for body weight and for milk yield (expressed in terms of butterfat yield). Instead of plotting the absolute values for weight and for butterfat yield (which would be more confusing on account of the two axes that such a chart would have), the values were plotted in terms of percentages of the mature values ( $A$  in equation 1). The numerical data for the weights and yields are given in Res. Bul. 96 of this series.

ous agricultural experiment stations in this country, were kept under conditions which were somewhat more favorable than those ordinarily found in commercial herds operated solely for milk production. The animals did not, however, receive the care given to animals on advanced registry test. Animals on test are, for example, milked three to four times a day while animals not on test are milked but twice a day. The rations, too, are usually better balanced, more appetizing, and in general more liberal in every way than in the case of cows not on test.

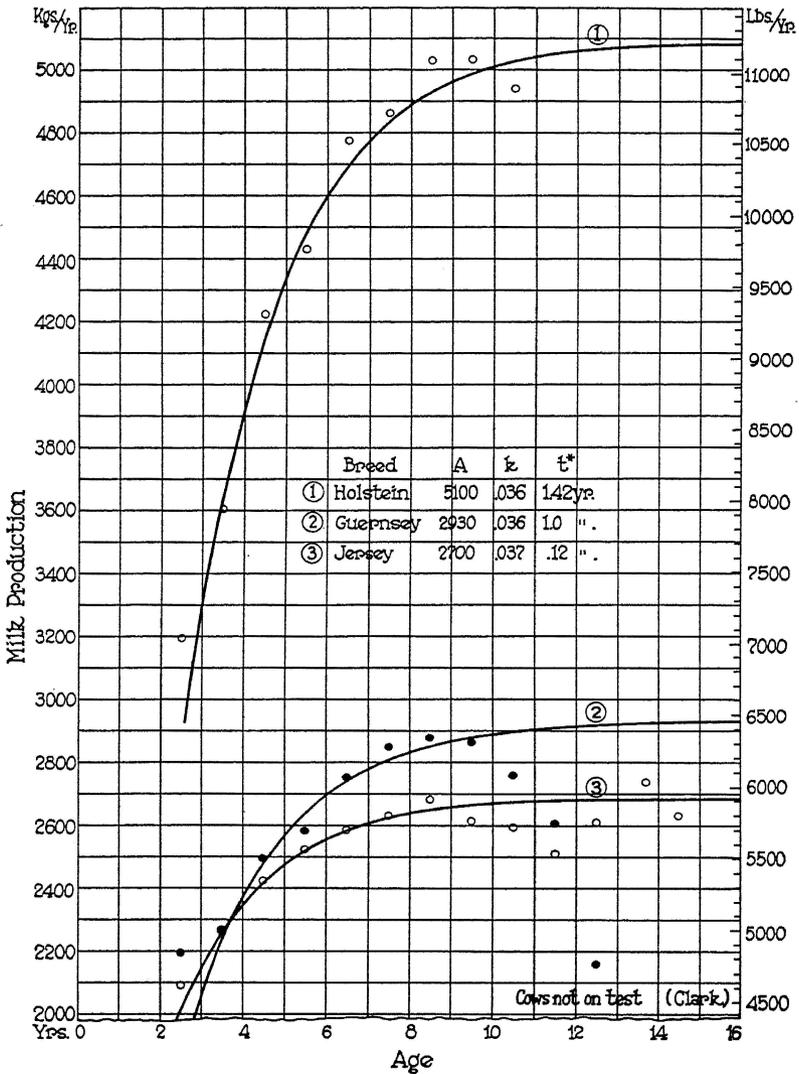


Fig. 4.—Milk production at different ages in three breeds of cows not on test (plotted from data compiled by R. S. Clark). Circles represent observed values, smooth curves represent equation (1) with the values of constants indicated on the chart. This chart shows that in Holstein cattle milk production approaches 5100 kilograms (i. e., 11240 pounds) per year as a limit. Following the age of 9 years, the observed values fall below the computed values on account of the process of senescence, which equation (1) does not take into account. The numerical values of  $k$  are the same for all 3 curves; this means that the speed of approach to maximum production is the same for all breeds. This does not, however, mean that all three breeds reach maximum production at the same age, for the values of  $t^*$  differ.

Fig. 4 indicates a satisfactory agreement between observed and computed values up to 9 years (which is the maximum age under consideration). Following 9 years, the milk yield shows a decided decline while the curves of equation (1) are approaching the maxima indicated by  $A$  as limits. The numerical values of  $k$  (the fractional decline in the increases) appear to be the same for the three breeds of animals, namely .036, or 3.6 per cent per month. The numerical values of  $t^*$  (age counted from birth at which the curve meets the age-axis) should perhaps be considered as age parameters of no significance in this connection even though it is possible to place an interpretation on them.

The milk yield during the first lactation period is somewhat above the computed values. This discrepancy between observed and computed values may possibly be a consequence of nutritional circumstances. During the period of milking, dairy cows are usually in negative equilibrium, certainly with respect to calcium metabolism. It is possible, therefore, that on the average, it is only during the first lactation period that the animals begin with the full reserve of the limiting factor (e. g., calcium), and that at the succeeding lactations the milk yields fall somewhat below the expected level because of the limiting factor in metabolism.

Fig. 5 represents the rise in milk yield (expressed in terms of butterfat yield, since the butterfat is commercially, the most important product), of several breeds of cows on Advanced Registry test. As pointed out before, not only are animals on test (usually) genetically superior with respect to milk production to animals not on test, but they are also given better care. The degree of agreement between observed and computed values is of the same order as in Fig. 4. The numerical values of  $k$  are, however, much higher in the present case than in Fig. 4. It appears to be a general rule that cows on test have a higher value of  $k$  (rate of approach to maximum yield) than cows not on test.

The higher value of  $k$  (which usually implies earlier maturity) in cows on test may be accounted for by the better environmental conditions, and particularly by the better food supply offered to the animals on test. That the rate of growth can be accelerated even in animals in apparently good nutrition was recently demonstrated by the remarkable results of Osborne and Mendel (J. Biol. Chem., 1926, LXIX, 661) which were confirmed by Dr. Hogan in this Station (Missouri Res. Bul. 96). Attention was also called to this matter in the sixth and seventh bulletins of this series (Res. Buls. 101 and 102) in comparing the growth curves of Norway and Albino rats, and the growth curves of the guinea pigs raised by Minot and by Castle.

An interesting example illustrating what effect management (nutrition) may have on the values of  $k$  and  $A$  is shown in Fig. 6. This figure which represents the data for purebred Register of Merit Jersey cattle

only, shows that the numerical values of  $A$  and  $k$  tended to increase from 1900 to 1923. While this increase is most probably attributable to better management due to increased knowledge of nutrition, there is, of course, some possibility that selective breeding may have contributed to the increased value of  $k$ .

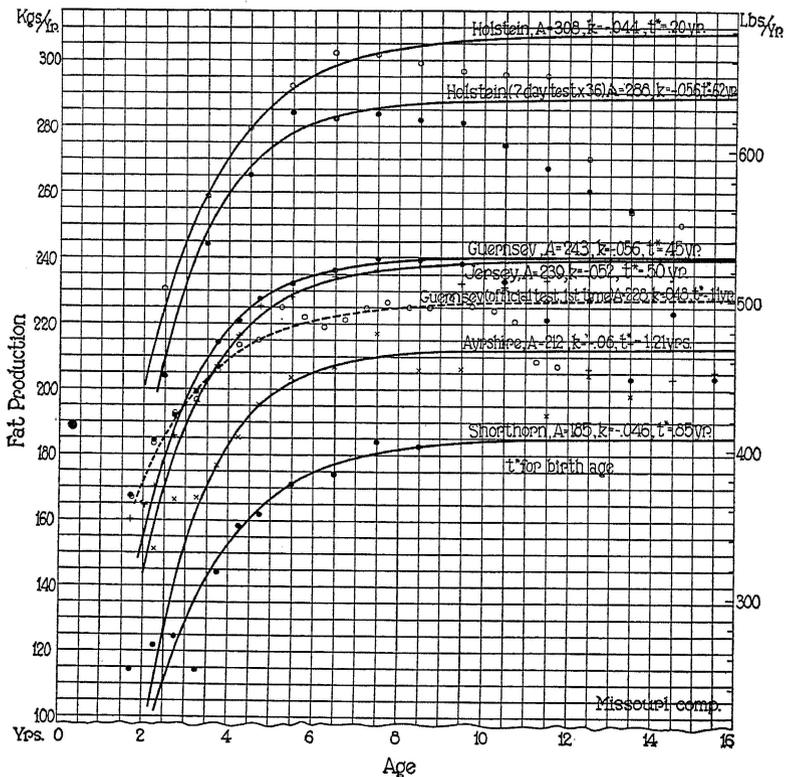


Fig. 5.—Milk production (in terms of butterfat) of cows on Advanced Registry test. The symbols represent observed values, the smooth curves represent equation (1). For further explanations consult the legend to the preceding figure, and the text.

The curve based on the compilation by Graves and Fohrman represents only the first records on test of the animals included in the other curves of the same chart. This curve substantiates the claim of Graves and Fohrman that the records for the first test tend to fall below the average of all advanced registry records of the animals which are continued on test. (Possibly because only such animals are continued on test as give promise of bettering their preceding records.)

The effects of various conditions on the numerical values of  $A$  (maximum production) and on  $k$  (rapidity of approach to maximum production) may be demonstrated with the aid of equivalence charts, and with charts in which the productions at various ages are plotted as percentages of the maximum production,  $A$ . The method for preparing equivalence charts has been explained in the seventh bulletin of this series (Res. Bul. 102). A series of such charts is presented in the appendix, at the end of the bulletin.

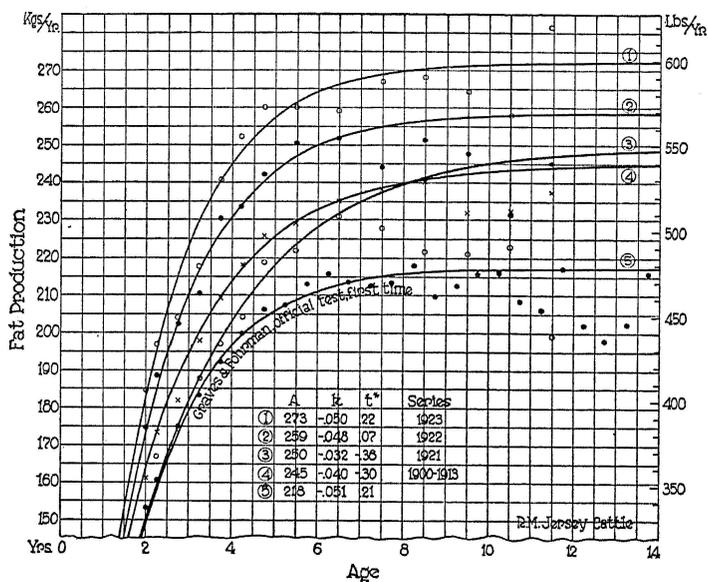


Fig. 6.—Age curves of milk yield for Register of Merit Jersey cattle during 1900-1913, 1921, 1922, and 1923. The animals in the latter series not only yielded larger quantities of milk (or butterfat), but they also appeared to approach the mature weight at a more rapid rate (i. e., they have a higher value of  $k$ ). Are these differences due to genetic or environmental conditions? The curve based on the compilation by Fohrman and Graves does not belong to this series, but was inserted to indicate that cows on test for the first time are significantly below in their production to the average production.

In the preceding charts the milk yields for a whole year (365 days) were plotted against age. On the following chart, Fig. 7, the milk yields for 7-day records are plotted against age. The data were obtained from the Holstein Advanced Register, which means that the production records were made under the best condition of management and at the time in the period of lactation when the milk flow is at a maximum (i. e., about one month after calving). For these reasons the records are not influenced by the depressing effect of the subsequent gestations as is often the case with yearly milk records, or by other complications in-

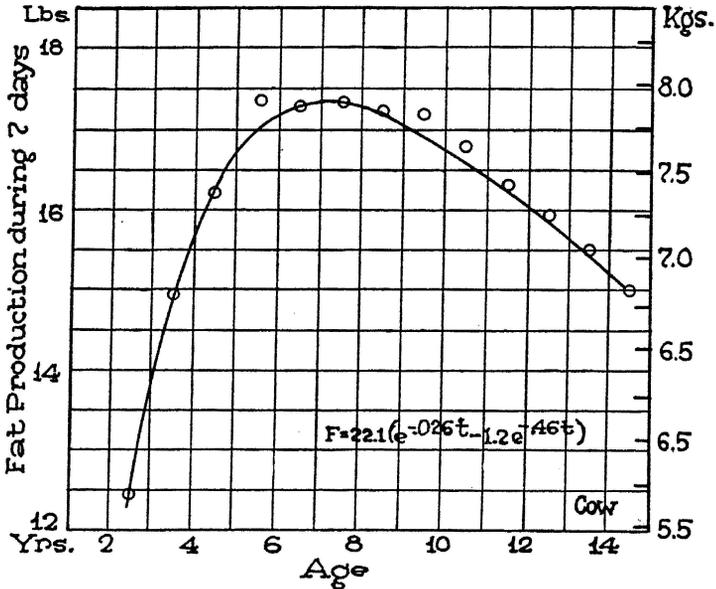


Fig. 7.—The rise and decline of milk yield with increasing age as indicated by 7-day records from the Advanced Register of Holstein cows. The circles are observed values, the smooth curve represents the equation in the chart. The fit of the equation to the rising segment of the age curve of milk yield indicates that until the maximum, the milk yields follow the course represented by equation (1).

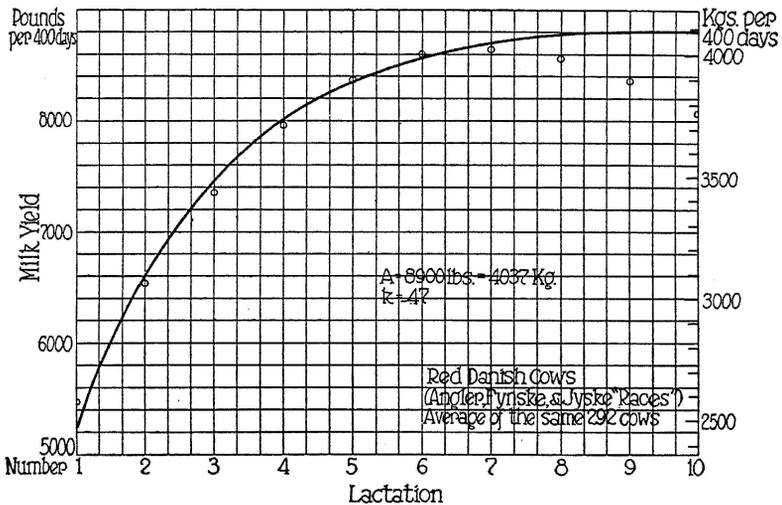


Fig. 8.—Changes in milk yield with successive lactation periods in Red Danish cows. The increments for the successive lactation periods are decreased by 47 per cent per year. That is, the increment in the milk yield for any lactation period is approximately one-half of the increment for the preceding lactation period. Assuming that each lactation period occupies 12 months, then the value of  $k$  on a monthly basis is  $\frac{.47}{12} = .04$ ; that is, the time rate of milk yield declines by 4 per cent per month.

herent in long-time tests (such as sickness and minor indispositions). In other words, if selective factors were not operating to diminish the size and to increase the quality of the population, these records would form ideal indices of the influence of age on physiological processes.

Finally, we present Fig. 8, for milk yield of Red Danish cows at different ages. These data (which were kindly transmitted to us by Dr. W. L. Gaines) have the merit of representing the *same* animals throughout the whole period of observation. While the ages of the animals are not definitely known (the milk yields are plotted against the corresponding numbers of lactations), they are not very important for the present purpose, as the number of lactation is directly proportional to age (one lactation corresponds, roughly, to one year). The value of  $k$  to be comparable to the  $k$ 's in the preceding charts, should be divided by 12 since in the preceding charts the values of  $k$  (fractional declines in the increases) were represented on a monthly basis, while the values of  $k$  in Fig. 8 were computed on the basis of a full lactation period (about one year). One-twelfth of the value of  $k$  in Fig. 8, namely .04, falls within the limits of the values of  $k$  in the preceding charts.

Before closing this section it is desirable to make a few historical references to investigations on age changes in milk yield.

As far as the present paper is concerned, the only work of interest from the present point of view is that of Pearl and his co-workers, for the reason that they were the first and, as far as the writer is aware, the only group of workers who published the results of a mathematical investigation on age changes in milk yield. Their first paper appeared in 1917. More detailed historical references (which have no direct bearing on the present work) may be found in McCandlish, Iowa Agr. Exp. Sta. Res. Bul. 73, 1922. A list of papers by Pearl, Gowen, and co-workers in the Maine Station is given in the bibliography of the first bulletin of this series (Res. Bul. 96).

What we wish to say about the work of Pearl, Gowen, and co-workers is that they used the following equations to represent age changes in milk yield.

$$\begin{aligned}
 y &= a - cx^2 + d \log x \text{ (Pearl and Patterson 1917, Maine Bul. 262)} \\
 y &= a + bx - cx^2 + d \log x \text{ (Pearl and Miner, 1919, Maine Bul. 279)} \\
 y &= a - bx - cx^2 - d \log x \text{ (Gowen, 1920, Maine Bul. 286)} \\
 y &= a + bx - cx^2 + d \log x \text{ (Gowen, 1920, Maine Bul. 293)} \\
 y &= a + bx - cx^2 + d \log (x - f) \text{ (Gowen, Milk Secretion, Baltimore 1924, p. 53).}
 \end{aligned}$$

In these equations  $y$  is the time rate of milk yield at the age  $x$ , while  $a$ ,  $b$ ,  $c$ ,  $d$ , and  $f$ , are constants. The fit of these equations to the data is satisfactory indeed. Our reason for proposing equation (1) does not represent a desire to devise a better-fitting equation, because, frankly, equation (1) does not fit the data as well as the equation of Pearl and

co-workers. Our purpose is rather to introduce an equation, the constants of which have well defined physical meaning. To the writer's mind, the constants of the equations of Pearl and co-workers do not have well defined physical meaning. The properties of the equation of Pearl have been discussed at some length in the third bulletin of this series (Res. Bul. 96) and in the *Journal of General Physiology*, 1927, X, 637, and they do not, therefore, call for further consideration at this time.

---

The data, and their sources, utilized in this section are presented in the dairy section of the first bulletin of this series (Res. Bul. 96). Some of the theoretical ideas presented in this section have been previously published by A. C. Ragsdale, C. W. Turner, and the writer in the *Journal of Gen. Physiol.* 1923, VI, 21.

### III. AGE CHANGES IN MILK YIELD DURING THE PERIOD OF CONSTANT BODY WEIGHT

The maximum in the age curve of body weight in dairy cattle is reached, roughly, at seven years. The exact ages at which different fractions of the mature body weights are reached in several groups of animals have been given in Res. Buls. 101 and 102 of this series. Following the age of 7-9 years, the milk yield tends to decline, while the body weight (as noted in the introduction) continues approximately constant. The decline in milk yield following nine years is particularly significant considering the fact that the poorer-milking cows are steadily weeded out with increasing age so that the records for the older animals represent an increasingly selected population. This more or less systematic elimination of the poorer milkers with increasing age results in an age curve of milk yield in which the data for different ages are not really comparable. For the present purpose, therefore, the available data on age changes in milk secretion are not entirely suitable.

Nevertheless, several years ago, A. C. Ragsdale, C. W. Turner and the writer attempted an analysis of the data for the purpose of relating the segment of declining milk yield with the segment of the rising milk yield (*J. Dairy Science*, 1924, VII, 189; *J. Gen. Physiol*, 1923, VI, 31). In the present bulletin we shall make use of these data and also of data kindly transmitted to the writer by Dr. W. L. Gaines, Chief in Milk Production at the University of Illinois.

In the present section we shall consider only the data following the age of nine years (or following the eight lactation periods), that is, the data constituting the declining segment of the age curve of milk secretion.

The numerical data on which these curves are based may be found in the Dairy Section of the first bulletin of this series (Res. Bul. 96).

The curves of these data are presented in Fig. 9a on an arithloggrid. Fig. 9a shows that the distribution of the data points about the straight line drawn through them is as good as might be expected, considering some of the aforesaid defects inherent in the data, and the small number of animals included in the declining segment of the curve.

For the yearly (365 days) records the value of  $k$  is between .03 and .04, which means that following the age of nine years the milk yields decline at the rate of 3.4 per cent per year. For the 7-day records, the decline is somewhat less—about 2.6 per cent per year. The difference in decline between the 365-day and the 7-day records suggest that (other conditions being the same) the persistency of milk secretion with the advance of the period of lactation decreases with increasing age. While we have no data on the relative decline of milk secretion with the advance of the period of lactation in aged cows, the proposition that older cows

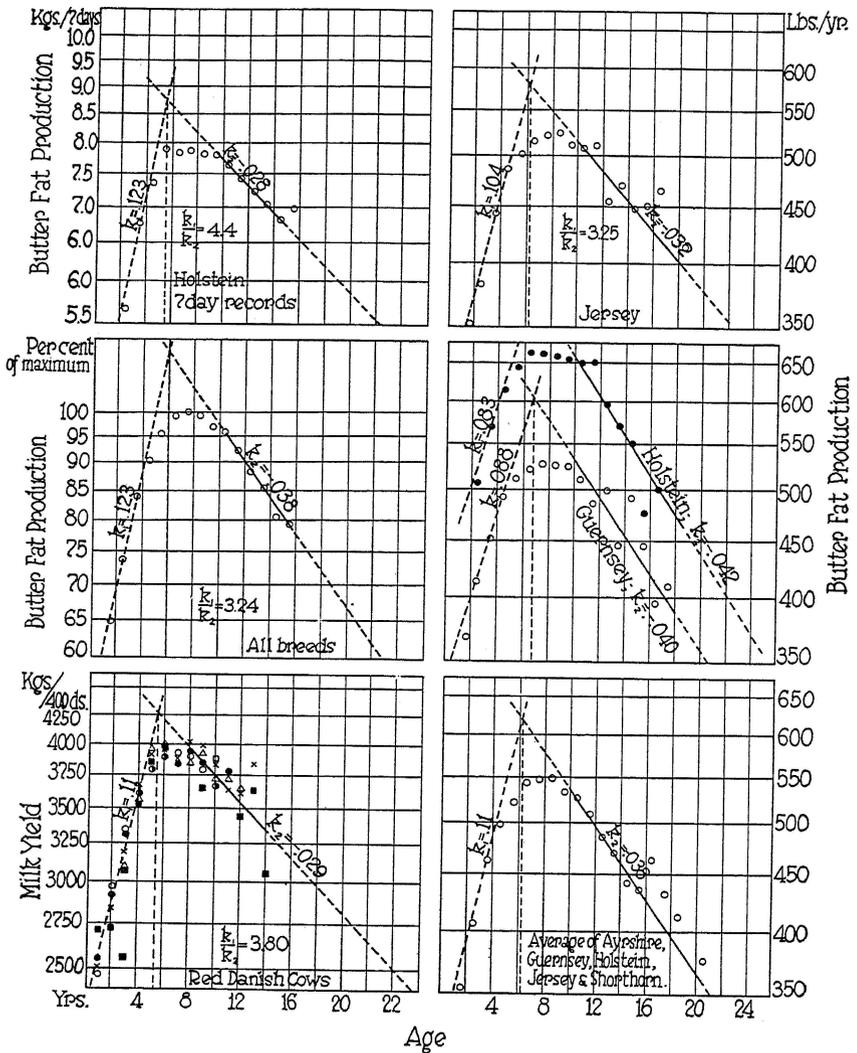


Fig. 9a.—The course of milk secretion with advancing age plotted on arithlog paper. In order to obtain the relative slopes of the rising and declining segments, straight lines were drawn (roughly) through the two segments of the curves. The quantity  $100k$  represents the percentage increase or decrease.  $\frac{k_1}{k_2}$  represents the ratio of the increasing to the decreasing slope. Vertical lines were drawn through the intersections of the curves to indicate in striking manner the asymmetrical nature of the curves. Ages are in years except for the Red Danish cattle in which case the numerals on the age axis refer to the number of lactation.

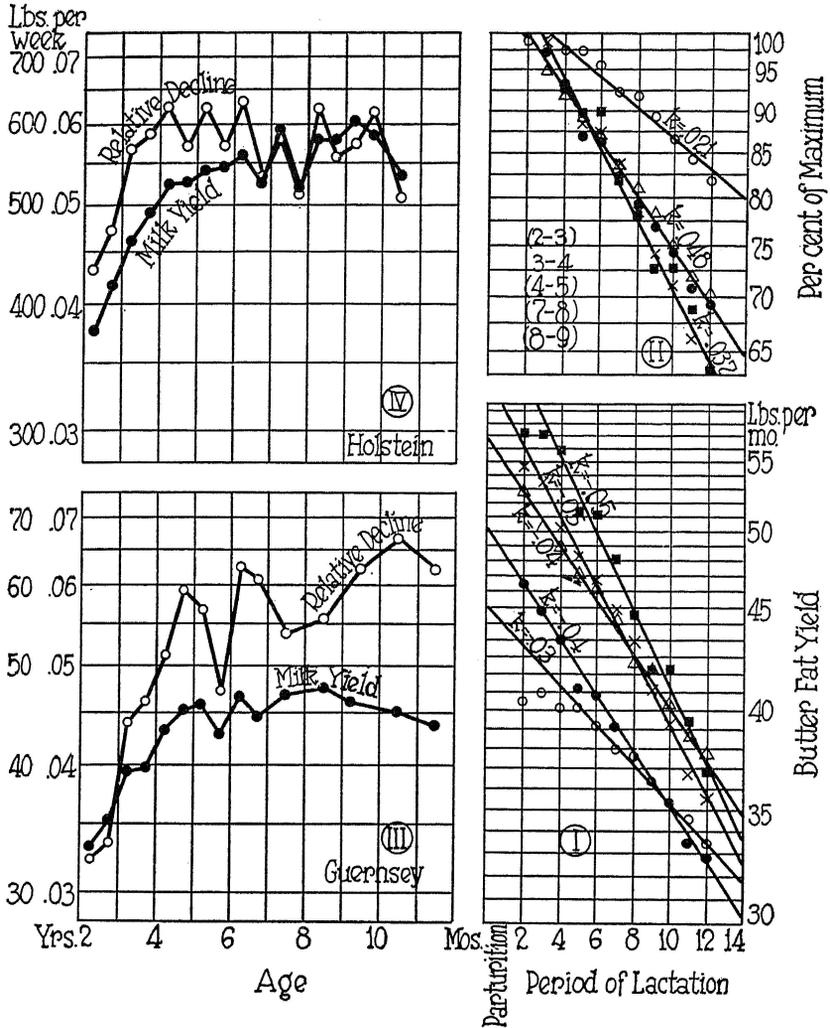


Fig. 9b.—The influence of increasing age on the decline of milk yield with the advance of the period of lactation. In I, the actual data were plotted on an arithlog grid. In II the data were first converted to percentages of the first month's production, then plotted on an arithlog grid. The numerals in parenthesis refer to the ages at which the declines with the advance of the period of lactation were observed. The charts show that there is an appreciable decrease in the values of  $k$ , relative decline of the milk yield, with the advance in the period of lactation with increasing age from 2 to 8 years. These increasing slopes appear, to a large extent, to be causally related to maximum (initial) yield rather than to age as such; that is to say, if the initial (maximum) yield remained constant with age, the decline  $k$  would probably also remain constant. This is indicated by III and IV in which the initial yield,  $A$ , (full circles) and the relative decline,  $k$ , (open circles) are plotted on the same arithlog chart. The two curves are nearly parallel. (cf. Turner, J. Dairy Sci., 1927, 10, 95; and Gaines, Univ. Ill. Agric. Exp. Station Bul. 288, 1927. I and II are based on data compiled in this Department by C. W. Turner. III and IV are based on data by Gaines.)

would be less able to keep up the milk flow with the advance of the period of lactation than younger cows is not unreasonable.

It would be interesting to compare these figures for the percentage decline (100%) as inferred from Fig. 9a, with the experience of dairy men. Unfortunately, few dairymen keep their animals after the age of 12 years. The present method of analysis is, to the writer's knowledge, the first to be published on the subject. It is possible that if the fact of the relatively small decline in milk yield with advancing age were brought to the attention of dairymen, they would be encouraged to keep their animals to more advanced ages. Of course, there are other reasons for the disposal of cows after 10 to 12 years, as for example the increasing irregularity in breeding which usually begins with 10 years and the deterioration of teeth which begins at about 12 years. Besides, dairymen raising their calves naturally prefer to keep the younger, possibly more promising, animals.

An interesting fact made evident by these curves and constants is the asymmetry of the age curve of milk secretion (*cf.* Fig. 9a and 7). Preceding the maximum, the decline in the increases of the time rates of milk yield was shown to be 36-68 per cent per year (3.0 to 5.6 per cent per month). Following the maximum, the decline in the time rates of milk yield is 3.0-4.0 per cent per year. Hence the decline in the *increases* of the time of milk yield preceding the maximum is 12 to 17 times as great as the decline in the time rate of milk yield following the maximum. In making this comparison it will, of course, be remembered that a severe selection is in operation during the life of the population, and that the older the population the more highly selected it must be. It is probable that the percentage decline in the time rates of milk yield would be much greater for a naturally non-selected population.

It may also be recalled that while the declines in the increases of the time rates of milk yield with increasing age, preceding the maximum body weight, are apparently related to the declines in the time rates of growth in body weight, the declines in the time rates of milk yield following the maximum in the curve are independent of changes in body weight. The slopes of the rising and declining segments of the age curve of milk secretion may therefore be limited by different, and possibly unrelated, mechanisms.

#### IV. CHANGES IN THE TIME RATES OF MILK YIELD WITH THE ADVANCE OF THE PERIOD OF LACTATION

As indicated in the introduction, there appears to be an essential similarity between the age curve of the organism as a whole and the time curve of development and decay of the milk secreting apparatus during a lactation period. In both curves we find a rising segment representing growth and development, in the narrower sense, and a declining segment representing senescence or decay. There is, of course, this conspicuous difference: The lactation cycles may be repeated several times in the life of the individual by the rejuvenating influence of pregnancy, while no rejuvenation is possible for the organism as a whole.

For the sake of simplicity we shall first discuss the properties of the segment of the lactation curve representing declining time rates of milk yield, then the segment representing the increasing time rates of milk yield, and finally the relation between the two segments.

**1. Decline in the Time Rate of Milk Yield with the Advance in the Period of Lactation.**—The time rate of milk secretion rises in the dairy cow during, roughly, the first month of the lactation period. Then it declines. In this section we shall confine our attention to the declining phase of the time curve of milk secretion which begins about one month after calving.

The data are plotted on arithlog paper in Fig. 10.

The data points (circles) for curve (2) in Fig. 10 fall on a perfectly straight line. The value of  $k$  indicates that for this group of farrow cows, the milk yields decline at a constant rate of 5.5 per cent per month. The data points (crosses) for curve (3) are likewise distributed about a straight line up to nine months, then there is a sharp decline. This sharp decline is, no doubt, caused by the fact that the cows were bred 3-4 months following calving and, as pointed out in the Dairy Section of the first bulletin of this series (Res. Bul. 96), 6-7 months after conception constitutes a critical period and the milk flow begins to be markedly depressed. The demand for growth and maintenance of the fetus becomes sufficiently great to reduce the total that the animal can spare for milk production (*cf.* Dairy Section of Res. Bul. 96). So the depression at the end in curve (3) and, to a less extent, in the other curves, should not be considered as a part of the normal (i. e., undisturbed) lactation curve.

On a whole, therefore, it seems safe to conclude that the general properties of the declining segment of the lactation curve are the same as the properties of the other senescence curves (Fig. 9a). The decline, to be sure, is very rapid—5 per cent per month is the same as 60 per cent per year—but the qualitative aspects of the two situations appear to be identical or at least, analogous.

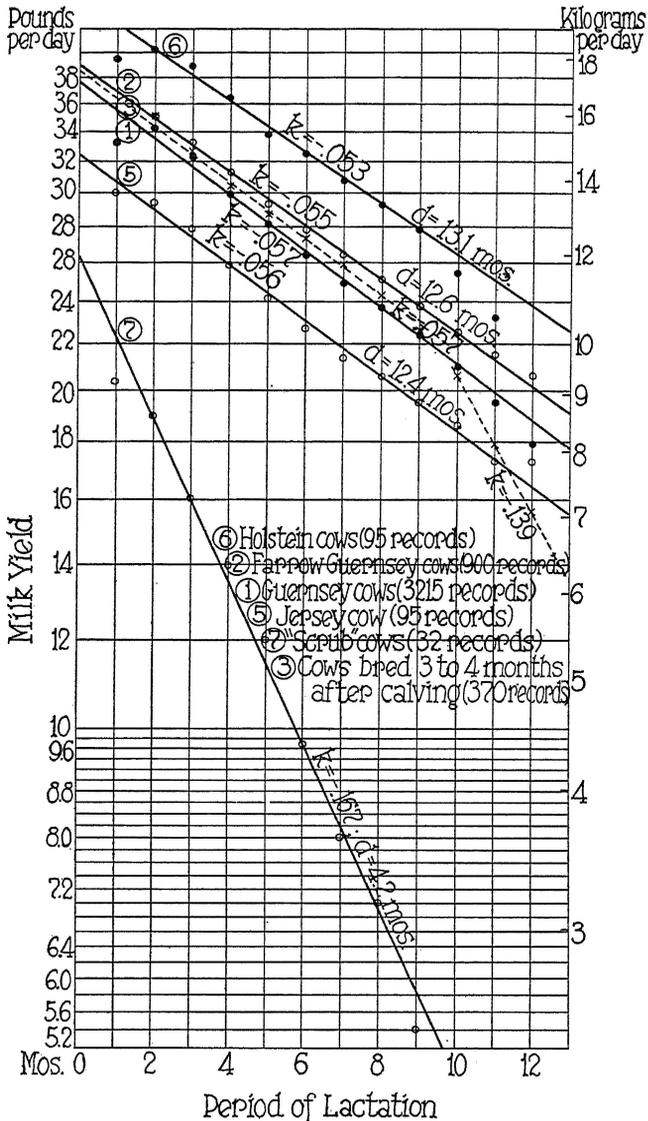


Fig. 10.—The decline in milk yield with the advance of the period of lactation of 6 groups of cows. The linear distribution of the data points on the arithlog paper shows that the decline takes place at a constant relative (or when multiplied by 100 percentage) rate indicated by the numerical values of  $k$ . With the exception of curve (2) which represents data on farrow cows, there is a decline, beginning with the tenth month of lactation. This decline is, no doubt, due to the depressing effect of pregnancy as demonstrated by the absence of such decline for the animals of the farrow group. The term  $d$  represents the time in months in which the initial level of milk yield is halved.

Curves (1), (2), (3), (5), and (6) in Fig. 10 represent the course of decline in highly developed dairy cows. In scrub cows, that is, cows not systematically bred for milk production, the decline is very much greater. For the scrub cow, represented by curve (7), the decline is almost 17 per cent per month, i. e., the relative decline is about three times as great as in the purebred cows. In beef cattle the decline is probably still greater. A good dairy cow is thus not only one which begins at a high level of milk production, but also one which declines from the initial level least rapidly (i. e., the value of  $k$  is small); in other words, one in which the persistency,  $(1 - k)$ , is high. The inheritance of persistency is, therefore, an extremely important practical matter to the dairyman. Fig. 11 indicates the total (theoretical) milk yield of which scrub and Advanced Registry cows are capable.

We shall now conclude this section with a brief historical note. In 1921-2 C. W. Turner, A. C. Ragsdale, and the writer attempted to formulate a "law" of decline in milk yield with the advance of the period of lactation. They found the equation.:

$$W = Ae^{-kt} \quad (2)$$

(in which  $W$  is the milk yield at age  $t$ ) to represent the data in a satisfactory manner. This result, as well as the data on which the curves in Fig. 10 are based, were published by them in several papers (J. Dairy Science, 1923, VI, 527; 1924, VII, 24; J. Gen. Physiol., 1923, V, 441 and 777). Equation (2) was made the basis of an extensive genetic investigation on the persistency of milk flow by Gaines and Davidson (see bibliography in Res. Bul. 96). Gaines and Davidson called attention to the fact (with which we were not familiar at the time) that Sturtevant, while he did not use any equation, nevertheless observed that the decline in milk yield from month to month tends to be constant (Report of the New York, Geneva, Agr. Exp. Sta. for 1886, pp. 21-23). Several other historical references which have some bearing on the present problem will be mentioned in Section 4 of the appendix to this bulletin.

**2. The Rise in the Time Rate of Milk Yield with the Advance of the Period of Lactation, and the Relation Between the Rising and the Declining Segment of the Lactation Curve.**—Fig. 12 represents the changes in the time rates of milk yield of three groups of cows during 90 days following parturition.

Fig. 11 shows that while the time rates of milk yield increase during the first 10 to 30 days after calving, the successive increments become less and less.

This observation suggests the possibility that equation (1) used to represent the course of growth in weight during the period following

puberty, and also the course of milk yield preceding 10 years, might also represent the rising segment of the lactation curve to equation (1).

The curve of equation (1) was accordingly drawn through the data points of the rising segment. The agreement between the theoretical (smooth) curve, and the data (circles) appears to be satisfactory. The quantity  $100 k$  represents the percentage decreases in the successive increments per day. Thus in the upper curve the increases in the time

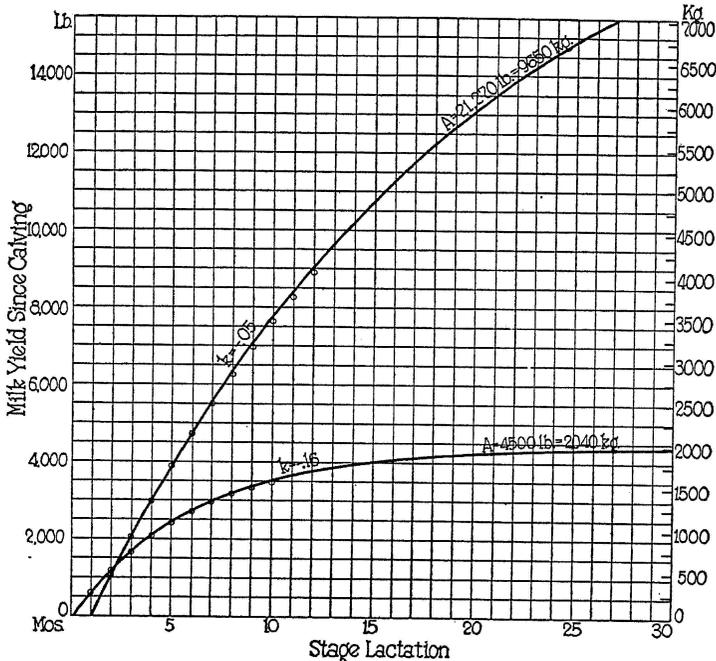


Fig. 11.—If the milk yields during a lactation period are added up, then we obtain a curve which may be represented by equation (1). The value of  $A$  represents the total which the animal is theoretically able to secrete during one lactation period if milking continues indefinitely. The circles represent the observed values on which curves (2) and (7) in Fig. 10 are based. See the section on limits in the appendix for further details.

rates of milk yield per day decrease by 10.8 per cent per day; in the lower curve by 34 per cent per day; in the middle curve by 19.3 per cent per day.

The value of  $A$  (37, 52.5 and 77) represents the *theoretical* (maximum) yield.

The values of  $B$  (29, 32, 33) are smaller than  $A$ , a fact which means that milk yield theoretically begins (and this is in reality the case) before calving.

A straight line was then drawn on the arithlog grid through the data points following 10-30 days after parturition, and the constants determined as before (Figs. 9. 10 and equation 2).

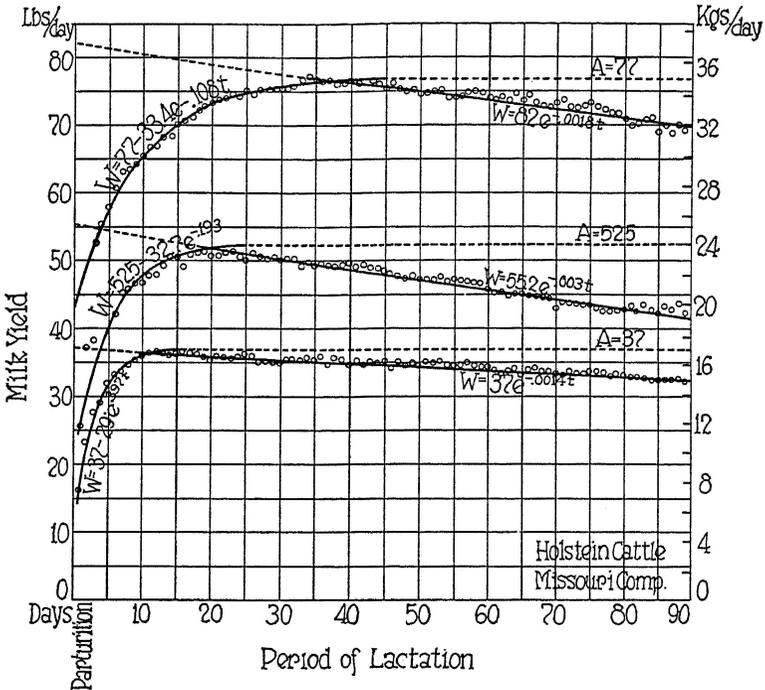


Fig. 12a.—The rise and decline in milk secretion with the advance of lactation of three groups of Holstein cows. The upper curve represents average milk yields of 47 cows milked 4 times a day. The middle curve represents the average yields of 32 cows milked 3 times a day. The lower curve represents 40 cows milked two times a day. The data were compiled by Mr. C. W. Turner of this (Dairy) Department (cf. Turner *et al.*, J. Dairy Sc., 1923, VI, 527).

The rising segments are represented by the equation

$$W = A - B e^{-kt} \tag{1}$$

The declining segments by

$$W = C e^{-k_2 t} \tag{2}$$

$W$  represents milk yield at time  $t$  after calving.  $A$  is the maximum milk yield.  $C$  is the theoretical yield at parturition obtaining by extrapolating the declining segment to zero time.  $k$ , is the (daily) fractional decline in the successive increases of milk yield for the rising segment.  $k_2$  is the fractional decline in the time rate of milk secretion for the declining segments of the curves.

The equations for the rising and for the declining segments may, of course, be combined into one as indicated on the chart, and one curve drawn as shown in Fig. 12b. The equation in Fig. 12b has the same form as the one employed by the physical chemist for representing the rise

and decline in the velocity of a process limited by two simultaneous consecutive reactions of the first order.

The form of the equation employed to represent the rising and declining course of milk yield with the advance in the period of lactation in Fig. 12b may also be used in the same manner to represent the rising and declining course of milk yield with advancing age as shown in Fig. 7.

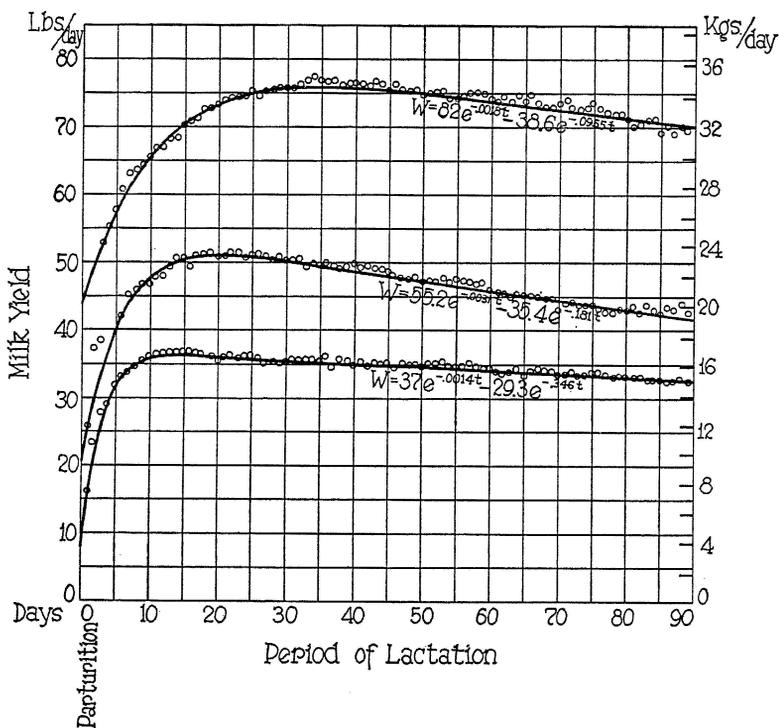


Fig. 12b.—The same data points as in Fig. 12a, but the smooth curves represent a combination of equations (1) and (2) of Fig. 12a, namely

$$W = Ce^{-k_1t} - De^{-k_2t} \quad (3)$$

The numerical values of  $C$  and of  $k_2$  are the same as in equation (2) of Fig. 12a.  $k_1$  is very roughly the difference between  $k_2$  and  $k$ , for Fig. 12a.  $D$  is not far from the value of  $B$  in Fig. 12a.

The applicability of the same equation to both curves indicates the presence at least of a quantitative similarity between these two processes, and it suggests the thought that the decline in milk yield with the advance in the period of lactation (following the first 30 days) represents a species of senescence in the mammary apparatus as truly as the decline in milk yield with advancing age (following 10 years).

## V. AGE CHANGES IN OTHER PHYSIOLOGICAL PROCESSES

We have found that during the period of growth in weight in dairy cattle, the time rates of milk yields and of growth follow the same course (equation 1). Following the period of maximum body weight, the time rate of milk yield declines at a constant percentage rate (equation 2), and the rising and declining segments of the age curve of milk yield may be represented by a combination of equations (1) and (2); that is, by equation (3).

We next proceed to substantiate the conclusions based on the analysis of data on the time relations of milk secretion by an examination of data on age changes of other physiological processes.

1. **Age Changes in the Time Rate of Specific Mortality.**—In Fig. 13a we have plotted specific mortalities of man against the corresponding ages. The data points are distributed along straight lines. The values of  $k$  (relative rate of increase) are given. Thus the specific death rates due to pneumonia increase with age at the rate of 5 per cent per year, or the specific death rates are doubled once in  $\frac{.693}{.05} = 13.9$  years. Similarly, death rates due to cerebral hemorrhage and apoplexy and diseases of the arteries, etc., increase at the rate of 12 per cent per year; that is, the specific death rates are doubled once in  $\frac{.693}{.12} = 5.8$  years. In other words, the circulatory system “ages”  $\frac{.12}{.05} = 2.4$  or  $\frac{13.9}{5.8} = 2.4$  times as fast as the respiratory system, but each, nevertheless, ages according to the same “law” as represented by equation (2). This “law” is, of course, that the *percentage* increase in senility (as measured by the increase in specific mortality) remains approximately constant from year to year within the ages of 20 and 70 years. The same type of reasoning applies to the other curves.

We do not quite presume to say that equation (2) represents a law of senescence not only because we do not know the details of the mechanism of senescence (the details of the mechanism of gravitation are not known, yet the statement for gravitational attraction is none the less a law), but also because we have made an assumption which can not be proved. We have assumed that the course of specific mortality is an index of the course of senescence of the organ, or system, under consideration. It seems reasonable to assume that, *all other conditions remaining the same*, the percentage mortality of a population should be proportional to the degree of its senility. It seems reasonable to assume that if two populations,  $A$  and  $B$ , are exposed to a given set of unfavorable

conditions, and if the degree of senescence of  $A$  is one half that of  $B$ , then the mortality of  $A$  should be one-half that of  $B$ . But the conditions of populations that we are considering are not the same. We may be considering populations of different genetic makeup at different ages. It

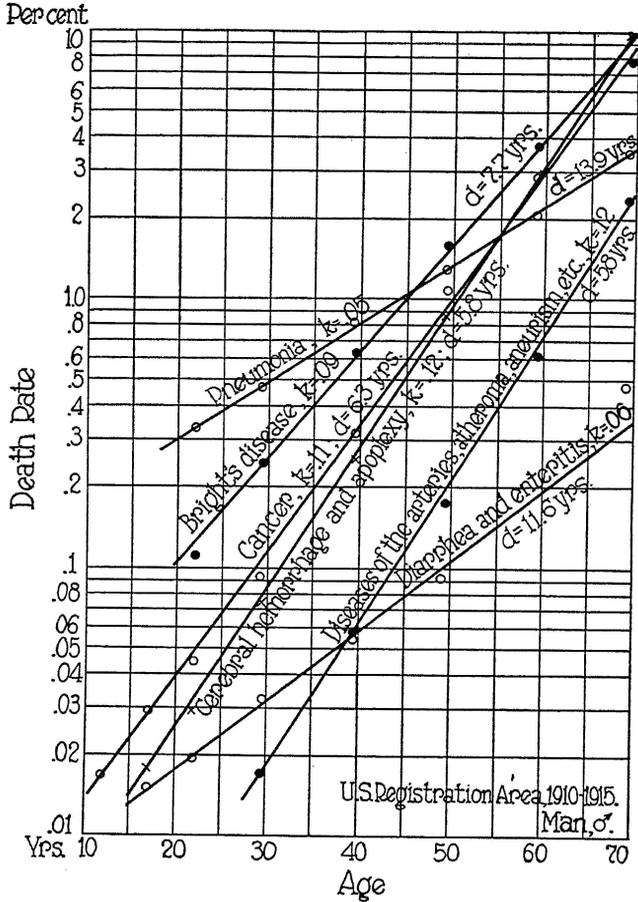


Fig. 13a.—The percentage, 100  $k$ , mortality of the given population of man appears to increase with increasing age of the surviving population. Thus the percentage mortality due to pneumonia increases at the rate of 5 per cent per year; or the mortality is doubled in 13.9 years ( $d$  represents the time in years in which the mortality is doubled). The increases in percentage mortality brought about by different causes are different; but for all the given causes the increases take place at a constant percentage rate as indicated by the linear distribution of the data points on the arithlog grid.

is possible, indeed probable, that the individuals of a poorer genetic resistance against unfavorable conditions are gradually weeded out, so that the older the individuals of a population, the more selected they are, with the net result that we are comparing populations of greater

genetic resistance against death at the more advanced ages, with those of lesser genetic resistance at younger ages. There are, however, these two compensating factors: first, the survivors at the later ages have been a part of the populations at the earlier ages so that, really, the populations are not entirely different; and second, the fact of survival implies not only that the survivors possessed greater ability to survive than those who failed to survive, but also that the unfavorable conditions which proved fatal to the less resistant individuals must have

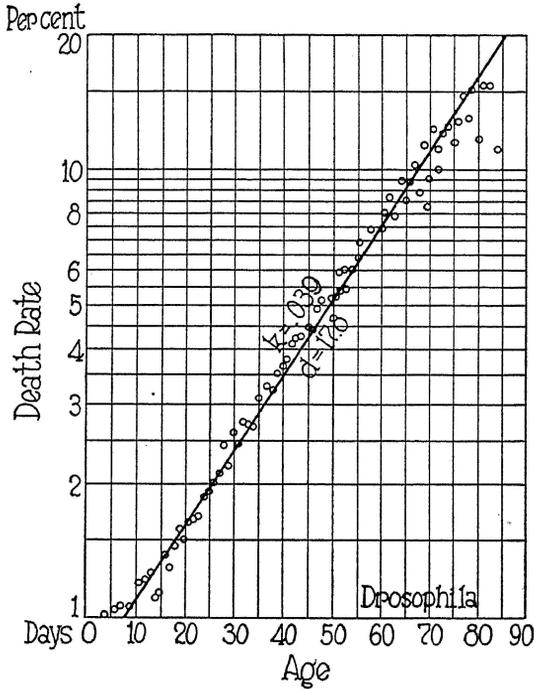


Fig. 13b.—The course of specific mortality in a population of *Drosophila*. (Data by Pearl and associates.) The specific mortality increases at an approximately constant percentage rate, namely 3.9% per day. (The specific mortality is doubled in 17.8 days.)

exerted an unfavorable influence on those that did survive, with the result that the surviving individuals did not survive as long as they might have if they had not been subjected to the earlier unfavorable conditions. Of course, the latter argument applies only to conditions the exposure to which does not increase, or produce, immunity. The specific mortality from diseases which produce immunity (as e. g., measles) of course, decreases with advancing age.

Our confidence in the course of specific mortality as an index of the course of senescence is increased by Fig. 13b indicating the course of

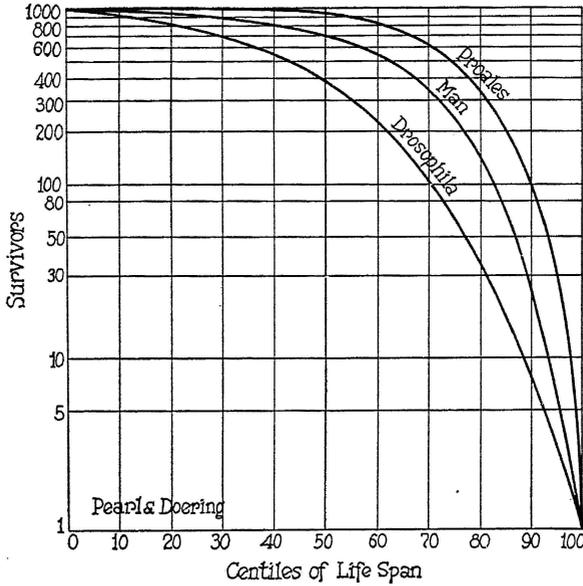


Fig. 14a.—The method of Pearl for comparing mortality curves of different organisms by superimposing two curves so that two biologically equivalent points coincide (after Pearl and Doering).

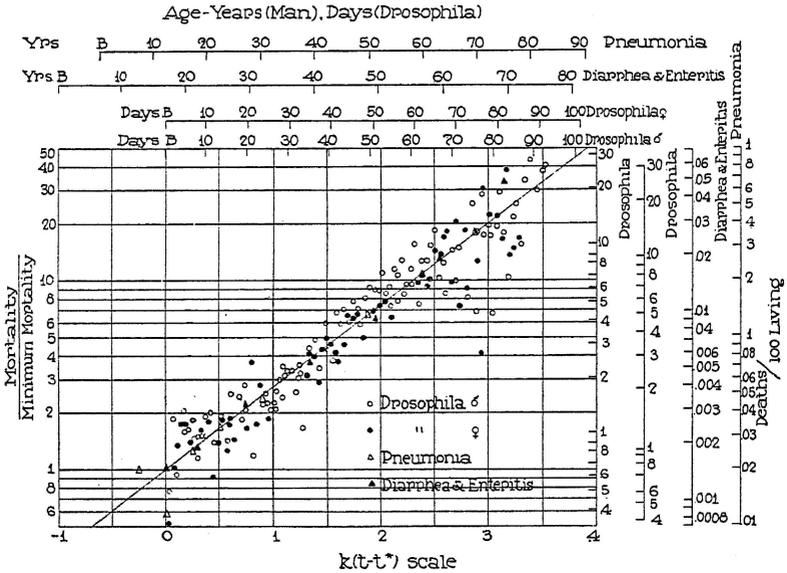


Fig. 14b.—A comparison of the course of specific mortality with increasing age in a population of man, and of a population of flies (*Drosophila*).

mortality of a population of the fruit fly *Drosophila*, a population which is genetically homogeneous, and which was kept under favorably uniform environmental conditions. The mortality data have been borrowed for the present purpose from Pearl's well known work on the *Biology of Death*.

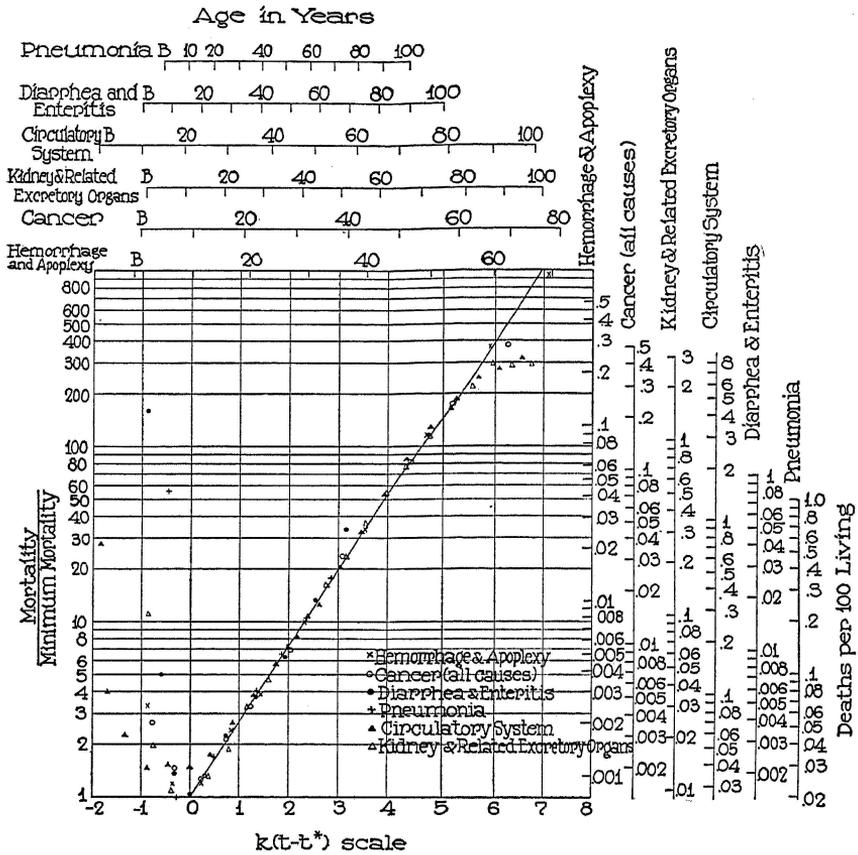


Fig 14c.—Equivalence between age curves of specific mortality in man due to the breakdown of different organs

While mentioning the work of Pearl we may recall that he published a method for comparing the mortality of certain lower organisms with that of man (Amer. Nat., 1922, LVI, 389; Science, 1923, Vol. 57, p. 209). This method consists in superimposing the two curves so that two biologically equivalent points coincide. The two points chosen are (1) age for each organism where the instantaneous death rate is a minimum, and (2) the age at which there is left but one survivor out of 1000 start-

ing at the minimum. For purposes of comparison, we have reproduced (in Fig. 14a) the equivalence chart by Pearl and Doering from *Science*.

It occurred to us (to Mr. H. H. Kibler, formerly a student and assistant, and to the writer) that a better agreement between mortality curves of different species could be obtained by employing the method of preparing equivalence charts explained in detail, in Res. Bul. 102 of this series. This consists in plotting the ratios of the mortality at the age  $t$  to the minimum mortality, against the  $k(t-t^*)$  scale in which  $t^*$  rep-

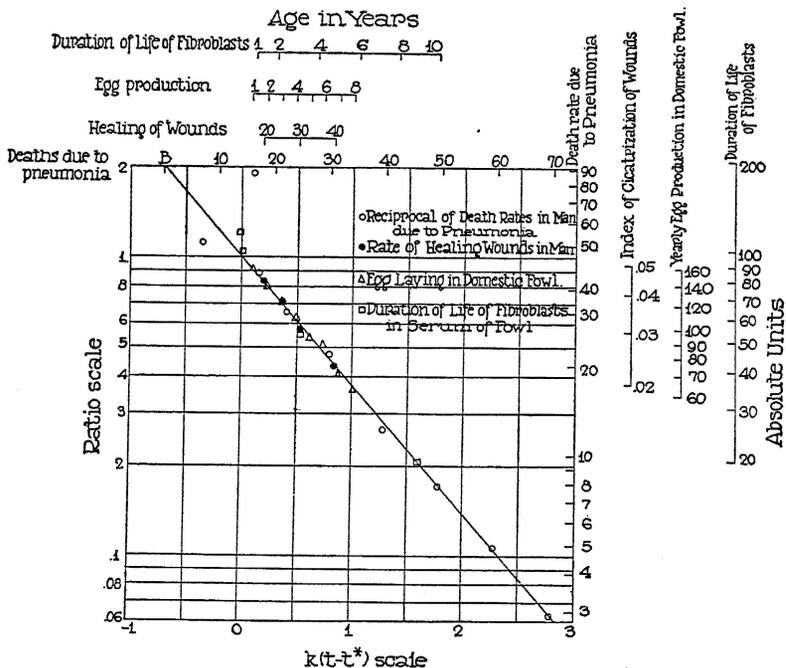


Fig. 14d.—Equivalence between age curves of senescence in man and in fowl.

resents the age of minimum specific mortality, and  $k$  is the relative increase in specific mortality as explained in connection with equation (1). The actual ages may then be inserted later.

The results of this idea are shown in Figs. 14b to d.

The fact that the different curves coincide so well substantiates the idea that the course of mortality has a lawful basis, and that it probably does represent the course of increasing senescence (i. e., decline in resistance to overcome unfavorable conditions of life with increasing age).

**2. Age Changes in the Time Rate of Ovation in the Domestic Fowl.**—Several years ago Henderson, Kempster and the writer pub-

lished (J. Gen. Physiol., 1923, VI, 41) a compilation of data on the decline in egg production with increasing age in the domestic fowl showing that the time rate of decline takes place at a constant percentage rate. Fig. 15 illustrates this fact. It may therefore be said that in so far as the course of egg production is an index of the course in decline of vitality (reciprocal of senescence), the degree of vitality of the domestic fowl

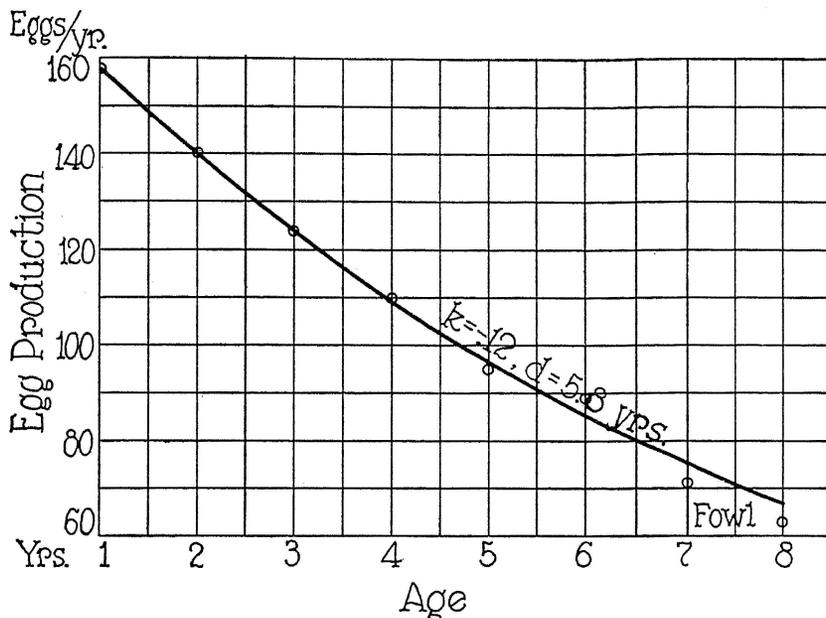


Fig. 15.—The time rate of egg production in the domestic fowl appears to decline at a constant percentage rate (12 per cent per year for this particular group). The value of  $d$  indicates that egg production is halved in approximately six years.

declines at the rate of 12 per cent per year; or what is the same, the degree of senescence increases at the uniform rate of 12 per cent per year.

It is not probable, however, that the course of egg production is an index of the course of senescence of the bird as a whole. If it were, the duration of life of the fowl would be not far from that of man, inasmuch as the value of  $k$  for mortality of man as determined by the breakdown of the circulatory system is also 12 per cent per year. Indeed, Fig. 14d indicating the equivalence between egg production in the fowl and mortality of man, shows the fowl at 8 years to correspond to man at 35 years, which is quite absurd. It is probable that the modern domestic fowl has been developed with respect to her capacity for egg production to an

extent which is out of proportion to the vigor of her other vital organs which might limit the duration of life.

3. **The Course of Healing of Wounds, and the Course of Duration of Life of Fibroblasts in *Vitro*.**—A somewhat more reasonable value of  $k$  for the decline in vitality or increase in senescence in the fowl is indicated in Fig. 16. In this figure the duration of life of fibroblasts grown in serum of chickens of different ages was plotted against the corresponding ages. This value of  $k$  is still low as indicated by Fig. 14d in

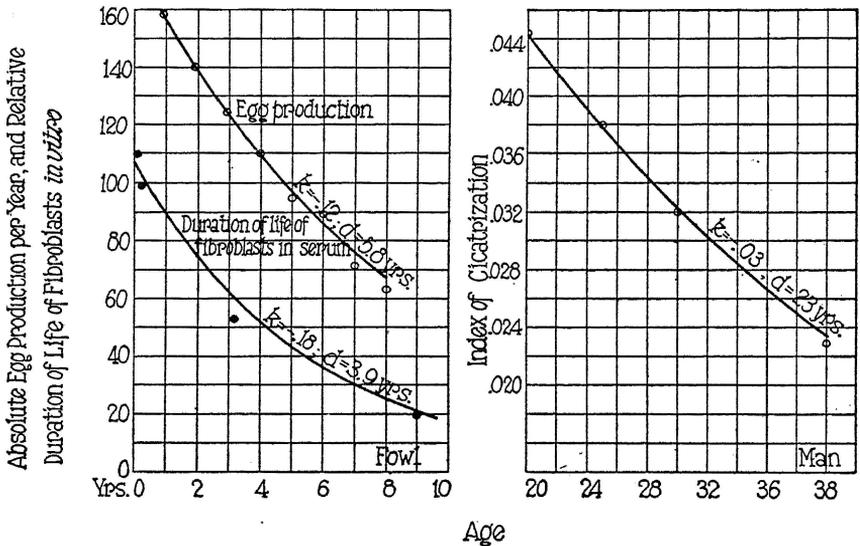


Fig. 16.—The age course of senescence in man as measured by the time rate of healing of wounds in man at different ages, and in domestic fowls by the time rate of egg production, and by the duration of life in fibroblasts grown in blood serum of chickens of different ages.  $100k$  represents the percentage decline for the unit of time indicated on the age axis.  $d$  represents the time required for any value to decrease to half; thus the time rate of egg production is halved in 5.8 years.

which the fibroblast axis (fowl) for 10 years corresponds to the pneumonia axis (man) for 50 years.

This equivalence between man and fowl becomes less probable if the comparisons are made with the course of mortality in man as limited, for example, by cancer or by the breaking down of the circulatory system. So the conclusion must be that the course of egg production and the course of duration of life of fibroblasts in chicken serum appear to follow an exponential law (equation 2), but that the values of the  $k$ 's of these curves are not direct measures of senescence in the sense of increasing rate of mortality with age.

The curve on the right of Fig. 16 representing the decline in the rate of healing of wounds in man with advancing age has a reasonable value of  $k$ . It will be recalled that the value of  $k$  for mortality curve for pneumonia is .05.

We are indebted to Drs. Carrel and DuNouy of the Rockefeller Institute for Medical Research for the data on healing of wounds and duration of life of fibroblasts *in vitro* (cf. the bibliography in Res. Bul. 96 for detailed references to the papers of these investigators).

**4. The Course of Senescence as Inferred from the Course of Basal Metabolism in Man.**—This section is concerned with the course of heat production (basal metabolism) in man during the portion of the life cycle following the period of growth in body weight (i. e., following the age of about 20 years).

The subject of change of basal metabolism with advancing age has been recently discussed in detail by Harris and Benedict (Publication 279 of the Carnegie Institution of Washington) and by DuBois (*Basal Metabolism in Health and Disease*). Our present purpose is, as previously pointed out, merely to substantiate our conception relating to the "law" of senescence for dairy cattle as formulated on the basis of an examination of milk secretion data.

According to this conception, when other conditions are the same, the time rate of heat production,  $H$ , should decline with age,  $t$ , by a constant relative (or when multiplied by 100 percentage) rate,  $k$ , as shown by equation (2).

$$H = Ae^{-kt} \quad (2)$$

The simplest way of testing the applicability of equation (2) to the data is to plot heat production,  $H$ , against age,  $t$ , on an arithloggrid. A linear distribution of the data points would justify an affirmative inference. If on the other hand the data are not distributed in a linear manner on arithlog paper, then we cannot be certain that equation (2) is not the "law" of decline of heat production with age for the following reasons. The basal metabolism is dependent not only on age but also (at least) on the following factors: 1. Body weight. 2. Body build (e. g., stature, bodily proportions, degree of fatness). 3. Genetic properties of the individual. Le Breton has recently called attention (Compt. Rend. Acad. Sc., 1926, CLXXXIII, 397; Ann. Physiol. et de Physicochem. Biol., 1926, II, 606) to the presence of species differences in the metabolism of warm-blooded animals, and there is no reason for assuming that no genetic differences in individuals of a heterogeneous population exist even when all other conditions are apparently the same. 4. Selective mortality of individuals at different ages resulting in comparisons of

relatively long-lived with relatively short-lived individuals. These complicating factors when taken with the facts that the observations for different ages were made on different individuals of different weights and build, and that the number of observations rapidly declines with age, make it evident that the resulting curve could not be expected to be very regular or to be fitted satisfactorily by any equation.

Harris and Benedict did propose preliminary "standards" of metabolism for different ages, but they point out that "in our opinion the time is not yet ripe for an undertaking of such magnitude" referring to the establishment of standards, and that "it seems desirable to analyze in a preliminary way the age changes." Harris and Benedict analyzed their data by the methods of statistical correlation without attempting to formulate rational generalizations on age changes in metabolism. DuBois' "standards" are likewise empirical, consisting in a set of values interpolated from a curve drawn, apparently free hand, through observational data.

The equation of Harris and Benedict relating metabolism to age is linear

$$H = C - at$$

in which  $H$  is the heat production at the age  $t$ .  $C$  is an empirical constant and  $a$  is the slope of the line passing through the data. That is to say, the *absolute* decline,  $a$ , in heat production, is assumed to be constant from year to year. In our proposed equation (2) the *relative* rate,  $k$ , of decline is assumed to be constant.

From a practical point of view it does not matter whether a linear or an exponential equation is fitted to the data. The reason for this practical indifference is that (*cf.* Res. Bul. 97) when the changes are slight, there is little difference between a linear and an exponential course. There may, however, be some theoretical reasons for preferring an exponential equation: (a) It seems more reasonable to assume that the decline in metabolism at a given age should be proportional to the metabolism *at* the given age as indicated by equation (2), rather than that the metabolism should decline from year to year by a constant amount. There seems no reason for assuming that the metabolism in a person of 20 years should decline per year by the same number of calories as in a person 80 years of age. (b) The constant  $k$  in equation (1) is a relative number and its value for metabolism could therefore be compared with the values for other age changes and for different species, as age changes in milk secretion, physical strength, vital capacity, etc. (c) Finally, if metabolism is a physico-chemical process, which it must be by definition, then it would be well to represent its time changes by the same equations

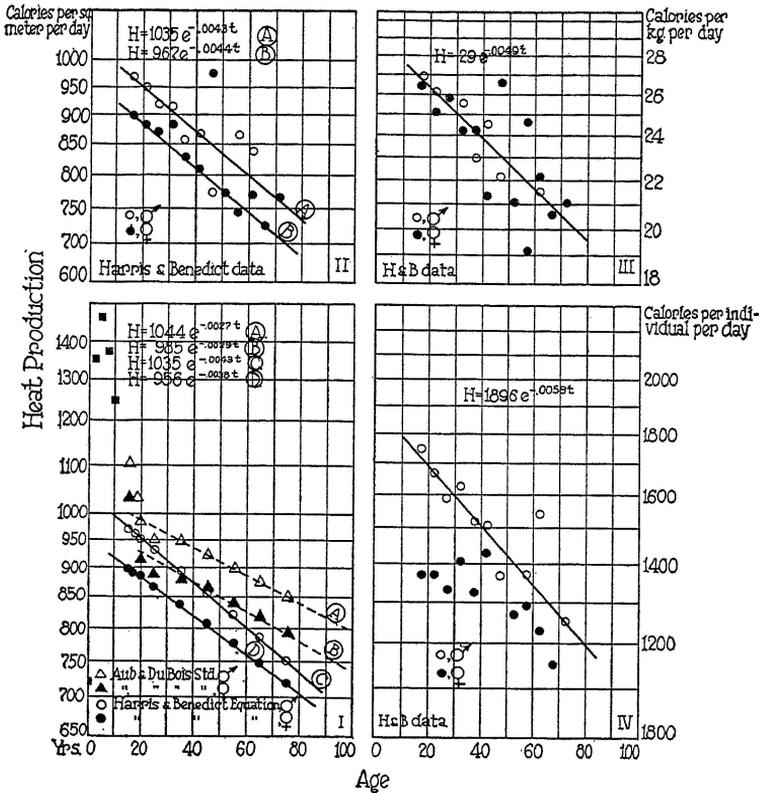


Fig. 17.—The course of basal metabolism in man with increasing age as it appears on an arithlog grid. This chart is based on numerical data given on pp. 123 and 118 of Publication 279 Carnegie Institution of Washington, 1919, by Harris and Benedict. I represents the data on p. 123 including the Normal Standards of Aub and Du Bois ("Sage Normal Standards": cf. p. 200 of the second edition of *Metabolism in Health and Disease* by DuBois) and metabolism as given by the equation of Harris and Benedict. II, III, and IV are based on the data on p. 118. The straight lines in II, III, and IV were drawn free-hand by the writer. The circles, etc., in II, III, and IV represent the observed values for metabolism as determined by Benedict and associates.  $100k$  represents the (yearly) percentage decline in metabolism with increasing age as determined by the writer. The equations represent the straight lines.

Harris and Benedict assume that metabolism decreases with age in a linear manner; that is to say, the metabolism decreases by approximately the same amount per year at all ages for which their equation was fitted. According to Harris and Benedict, the total daily metabolism decreases on the average by 7.15 calories per year in men and by 2.29 calories per year in women; the decrease in daily metabolism per square meter of surface, as estimated by the DuBois height-weight chart, is on the average 3.60 calories per year for men and 2.96 calories per year for women. According to the writer's conception, *a priori* considerations suggest that it is not reasonable to assume that metabolism should decrease by the same absolute amounts per unit time in relatively very young individuals as in relatively very old individuals; and that it would be more reasonable to assume that the decline in metabolism at any time should be proportional to the metabolism at the given time; that is, the metabolism should decline from year to year by a constant percentage  $100k$ . This latter conception is represented by the given equations and straight lines on the charts.

as are used to represent time changes of other physico-chemical processes. Equation (1) is an equation of the simplest type (first order) used to represent time changes of physico-chemical processes.

Accordingly we have plotted in Fig. 17 several sets of metabolism data on arithlog paper and roughly estimated the slopes of the curves, that is the values of  $k$  in equation (2). The "standards" as well as the observational data were plotted. The significance of the resulting charts are indicated in their legends.

The relative rate,  $k$ , of decline in metabolism for man is surprisingly low—only 0.3 to 0.4 per cent per year when referred to unit of surface area. We have seen that the rate of increase in mortality with age due to the breaking down of certain organs, or organ systems, is very much greater. This relatively slight decrease may perhaps be attributed, in a small part, to the comparison of relatively few long-lived individuals at more advanced ages with many short-lived individuals at the earlier ages. It may perhaps also be attributed in part to a certain fallacy in representing the course of metabolism with age on the basis of unit area, weight, or stature. After a certain age there is usually a shrinking (sometimes fattening) of the body. There is certainly a decline in stature after 50 years of age, and also in weight at more advanced ages. By representing metabolism per unit weight, stature, or area, a given individual is therefore credited with a relatively greater metabolism, per unit weight or area for the more advanced ages than for the earlier ages—for his body is gradually shrinking. What was originally a unit of weight or area is steadily declining to a smaller fraction of the original unit. However, as far as the student of age changes in metabolism of man is concerned, he has no choice but to represent the course of metabolism per unit weight or area, because it is not possible to follow the course of metabolism of the same individuals throughout their lives, and it is not possible to compare individuals of different sizes at different ages without resorting to the use of area, weight, or stature.

## VI. SUMMARY AND CONCLUSION. THE RELATIONS BETWEEN GROWTH AND SENESCENCE

One conclusion that impressed itself during the course of this work is that both growth and senescence are examples of processes the time relations of which follow "the ubiquitous law of compound interest."

It was pointed out (equation 1, 2, and the preceding bulletins of this series) that the time relations of growth before and after puberty, as well as the time relations of senescence, may be represented by the same exponential law as is indicated by the aforesaid equations. These equations are all examples of the "law of compound interest." The applicability of these equations to the time changes of growth and senescence

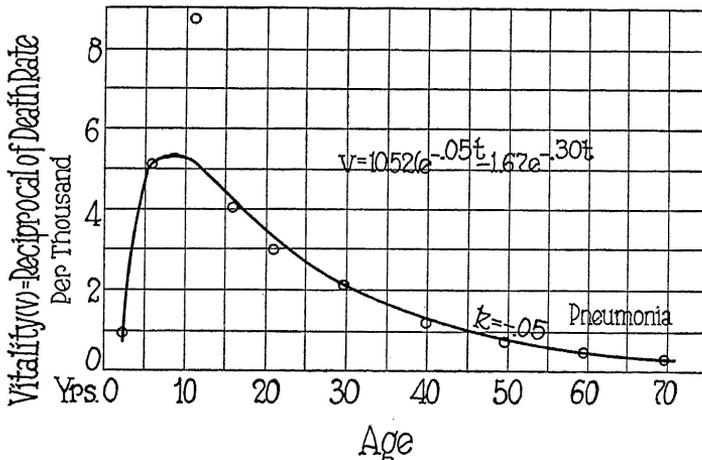


Fig. 18a.—The rise and decline of "vitality" with age in man (U. S. Registration Area) as measured by the reciprocals of death rate due to pneumonia. (The mortality data have been plotted in Fig. 13a.) Circles represent observed values; the smooth curve represents the equation on the chart.

means that the relative (or when multiplied by 100 the percentage) rates of change (increase in body weight before puberty; decrease in increments in body weight after puberty and increase in the degree of senescence, or decrease in vitality) are constant in all these cases.

The numerical values of the relative rates,  $k$ , of growth are senescence are, however, quite different. In the few cases that we have examined it appears that the relative rate of senescence (slope of the declining segment of the life curve) is less than the relative rate of growth (slope of the rising segment). That is, the value of  $k$  is smaller for senescence than for growth. This is only another way of saying that maturity (e. g., maximum body weight or maximum milk yield) is not reached in the middle of the life cycle, but perhaps at one-fourth of the

life cycle. Thus in man, the maximum body weight (as it may be attributed to growth and not fattening) is reached between 20 and 25 years, while the maximum duration of the life cycle is approximately four times this value. Similarly in the dairy cow, the maximum body weight is reached about 6 to 7 years of age and the maximum duration of the life cycle is approximately four times this value.

These estimates are of course very rough because the maximum or even the average age at death is not necessarily limited by the time relations of the processes that we have been investigating. The course of milk secretion in the dairy cow, or of ovulation in the domestic fowl, is not necessarily an expression of the course of senescence of the organ which is the limiting factor in the duration of life.

Since, however, there is some theoretical interest in determining the relations between the values of the  $k$ 's for the rising and declining phases of the life cycle, we present several charts giving the equations for the complete curves whenever possible.

It was already indicated that if the declining segment of the growth-senescence curve can be represented by the equation

$$W = Ce^{-k_2 t} \quad (2)$$

and the rising segment by

$$W = A - Be^{-k_1 t} \quad (1)$$

then the whole curve can be represented by combining the two equations thus:

$$W = Ce^{-k_2 t} - De^{-k_1 t} \quad (3)$$

The following considerations may make clear the reason for the theoretical interest attached to the fitting of equation (3) to the growth-senescence curve. As explained in the preceding bulletins of this series, particularly in Res. Bul. 97, equations (1) and (2) are essentially the equations of monomolecular change of the physical chemist. Since the processes of growth and senescence must, by definition, have a physico-chemical basis, it is tempting to generalize by saying that since the kinetics of growth and senescence can be represented by the equations representing the kinetics of chemical reactions of the first order, growth and senescence may perhaps be limited by chemical reactions of the first order. Similarly, equation (3) is the equation of two simultaneous-consecutive reactions of the first order, and if it should be found to represent the course of growth and senescence, we would naturally be tempted to generalize by saying that the course of growth and senescence tends to be limited by two simultaneous-consecutive reactions of the first order. (For an exposition of the theory of consecutive-simultaneous reactions, see Lewis, *A System of Physical Chemistry*, Volume 1, p. 402, 1920 edition; Mellor, *Chemical Statics and Dynamics*, p. 96; and books on radio-active transformations.)

In presenting this discussion and the charts we do not wish to give the impression that the fit, or misfit, of equation (3) to the data can be taken to constitute proof or refutation of the idea that growth and senescence are limited by certain physico-chemical reactions. If it

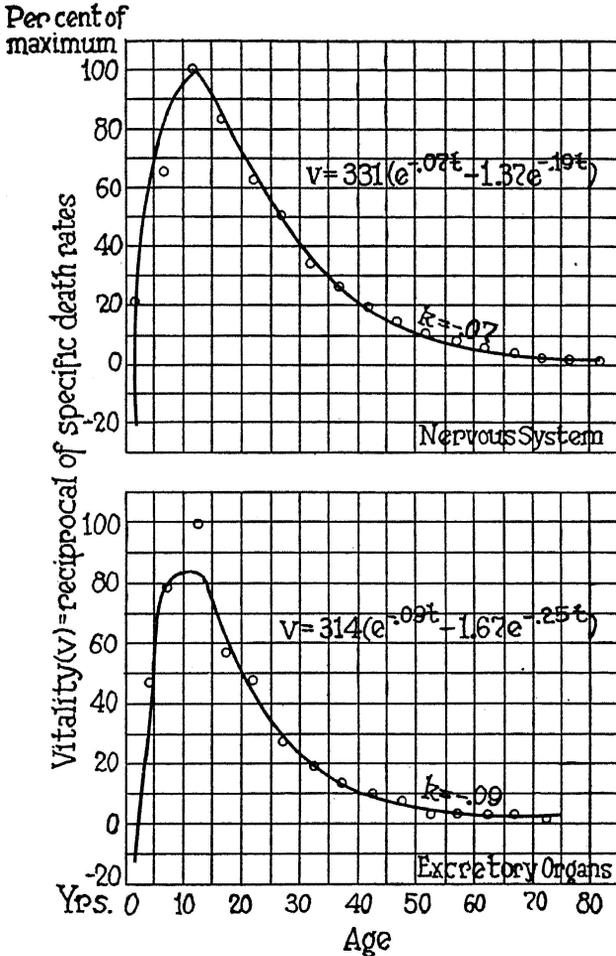


Fig. 18b.—The rise and decline of "vitality" in man with increasing age as measured by the breakdown of the nervous system, and excretory system. Compare to Figs. 13a and 18a. The data are represented as percentages of the maximum values.

were possible to prove or to refute theories by a fit of a certain kind of equation, the proof of theories would be a much simpler matter than it is. The writer's uncertainty concerning this matter is evidenced by one statement in the text that the mechanisms limiting the course of growth

may not be related to the mechanism limiting the course of senescence. What we wish to do is to make a small contribution toward the formulation of some quantitative statement of the situation.

The curves that we have prepared are shown in Figs. 18a to 18d. The equation and other pertinent information are given on the charts and in the legends to the charts, and so need not be discussed in the text.

Before closing this section it seems desirable to discuss the justification for assuming that the rising and declining curve of milk yield with the advance of the period of lactation (Fig. 12) represents a species of growth and senescence and that it may be analyzed in the same manner as curves of growth and senescence. In case no justification is called for (the terms growth and senescence may, of course, be applied to any process involving development and decay) then it is desirable to bring in line the unique properties of the lactation cycle with other similar phenomena in biology.

In the first place there is an undoubted similarity between the shape of the lactation curve and the growth-senescence curve as indicated, for example, by the rise and decline of milk yield with advancing age (Fig. 7). While such a similarity in the shape of curves cannot be considered as a criterion of similarity of causal mechanisms, it is nevertheless very suggestive. The mammary gland obviously grows and develops during gestation, then it obviously declines in size and undergoes retrogressive changes. Is not this similar to the process of growth and senescence of the body as a whole (*cf.* Figs. 7 and 18)?

The unique fact about the lactation cycle is that it is recurrent. The mammary apparatus is, so to speak, "rejuvenated" by the successive pregnancies. (Occasionally milk secretion is initiated by causes other than pregnancy; *cf.* e. g., Velich, *Lait*, 1926, VI, pp. 1 and 102.) This is a unique phenomenon, yet not the only one known. Ovulation in mammals, and more strikingly in birds, is a periodic process. How is this type of "rejuvenation" brought about?

It was already mentioned in the introduction that under certain conditions, and in certain species of animals, it is possible to rejuvenate, in the sense of rendering young again, the whole organism as shown in Fig. 1. Childs planarians have been oscillating between the juvenile and adult stages, and theoretically these cycles may be continued perhaps indefinitely. In Childs planarians food served as the rejuvenating factor. In the case of the mammary apparatus some factor, the nature of which is not known, probably plays a similar role, and the situation in the two cases appears to be quite analogous. Fig. 19 indicating a quantitative relation between the duration of the period

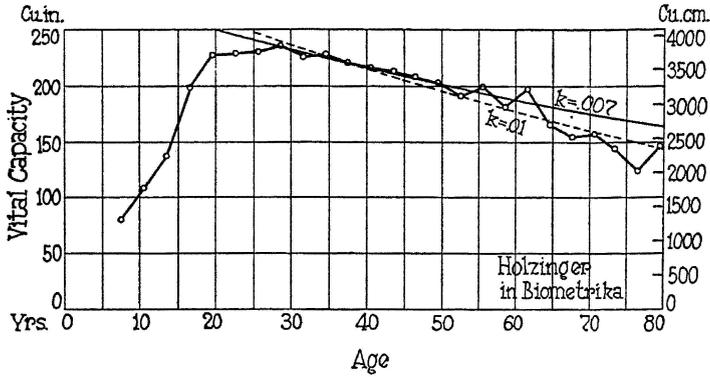


Fig. 18c.—The rise and decline of "vitality" in man as measured by the rise and decline of vital (lung) capacity. Between 28 and 65 years the vital capacity appears to decrease at the rate of 0.7 per cent per year (a slightly greater value than that for the percentage decline of basal metabolism indicated in Fig. 17). If equation (2) is fitted (by compromise) so as to include the period between 30 and 80 years, then the decline increases to 1.0 per cent per year (broken curve). However, the data following 65 years are probably not sufficiently reliable for inclusion in the fitting of the curve, and the smaller value of  $k$  is probably the more reliable of the two.

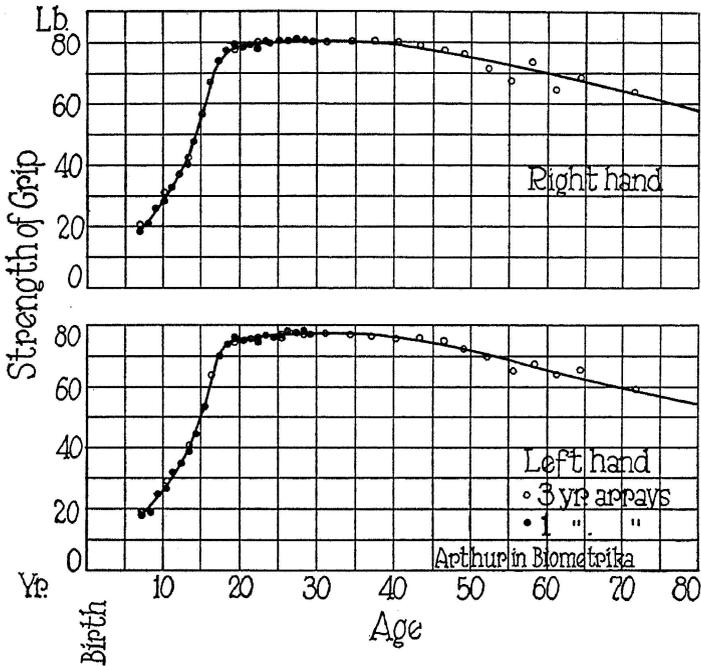


Fig. 18d.—The rise and decline of strength of grip with increasing age. The nature of the distribution of the data does not permit an evaluation of its constants from the present point of view, but this graph will be of interest as a reference in connection with a future bulletin of this series, and as showing that the maximum is reached between 20 and 30 years.

of gestation and subsequent milk yield, may be considered as substantiating evidence for the idea that there is a production of some rejuvenating factor during the course of gestation.

The rise in the milk yield  $M$  following parturition may be explained by assuming that the production of the rejuvenating factor (secreting cells or possibly some other factors) does not cease with parturition. It may also be explained in a more elaborate manner on the basis of the assumption that the course of growth is limited by the transformation of a factor  $A$  to  $M$  according to equation (1).

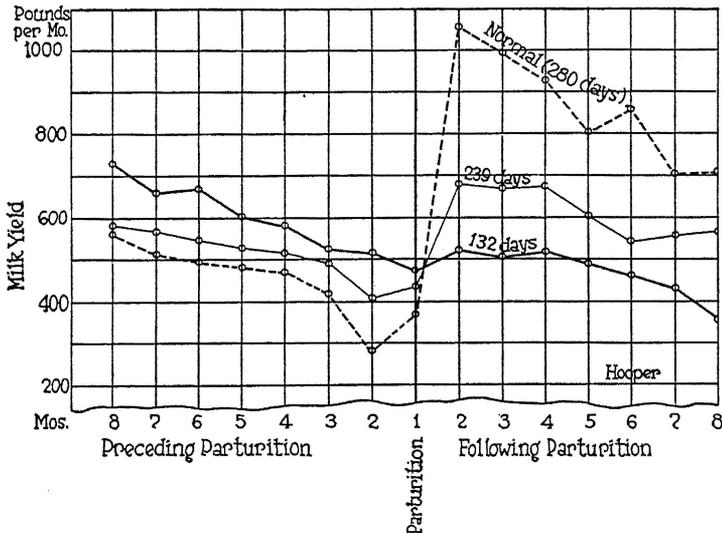
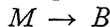


Fig. 19a.—The rise and decline in the time rate of milk yield following parturition when the preceding gestation periods are of different lengths. A gestation period of 280 days resulted in a much higher milk yield than gestation periods of shorter duration (239 or 132 days). This fact suggests that there is a quantitative relation between the length of the gestation period (during which the mammary gland, and possibly some other factors limiting milk production, is developed) and milk production; and that the periodic rejuvenation of the mammary gland is dependent on the production, directly or indirectly, by the pregnant uterus of some rejuvenating substance or substances. (Modified from Hooper.)

and the course of senescence (decline in milk yield) is limited by the transformation of  $M$  to  $B$  according to equation (2).



on combining the two processes we obtain the transformation according to equation (3).



In the case of milk secretion following parturition, factor  $A$  becomes available for transformation into  $M$  (the limiting factor in milk

production). The speed of production of  $M$  is proportional to the concentration of factor  $A$ , and the speed of disappearance of  $M$  is proportional to the concentrating factor  $M$ . At the beginning of the milking period (parturition) we have a high concentration of  $A$  and a low concentration of  $M$ . Hence the amount of  $M$  accumulates at a greater

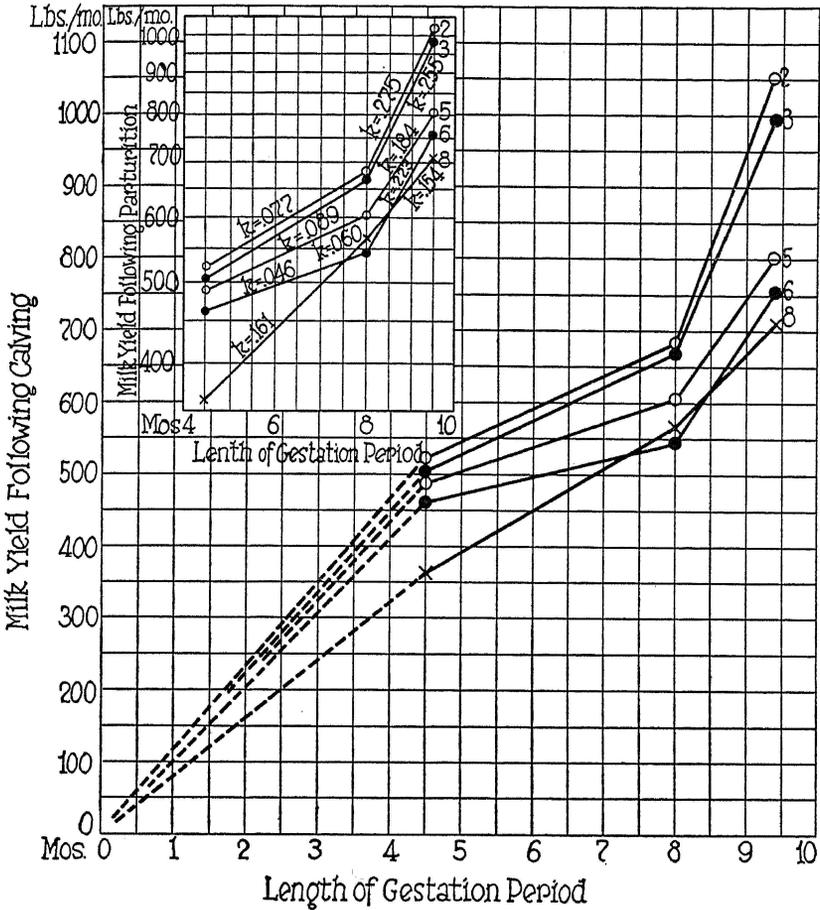


Fig. 19b.—The relation between the milk yielded during the 2nd, 3rd, 5th, 6th, and 8th month of the lactation period indicated by 2, 3, 5, 6, 8, on the chart and the duration of the preceding gestation period. The insert shows the same data plotted on arithlog paper.  $100k$  indicates the monthly percentage increase in milk yield with the increase in the length of the gestation period (plotted from data by Hooper). Each curve represents the average of 6 cows. It appears that the percentage rates ( $100k$ ) of increase in milk yield as well as the time rate increase with the increase in the length of the preceding gestation period.

time rate than its disappearance, resulting in a rising and declining curve of  $M$  (milk yield) which is quite typical of the majority of the curves of transformation as a result of simultaneous-consecutive re-

actions. The same ideas may, of course, be utilized in explaining the shape of other curves of growth and senescence.

The latter explanation, which was previously published by A. C. Ragsdale, C. W. Turner and the writer (*J. Gen. Physiol.*, 1924, VI, 541), was criticized by Gaines and Davidson (*J. Gen. Physiol.*, 1926, IX, 325). They suggested that it would be more reasonable to explain the rise in milk yield following parturition as representing a recovery process from a hypothetical "hormone thrown into the circulation during pregnancy and acting as an inhibitor to milk secretion. . . It is assumed that the source of the inhibitor is removed with the birth of the fetus so that the supply of the maternal circulation is cut off abruptly at parturition. A certain amount of inhibitor is at that time left in the maternal body and gradually disappears." It is clear that the end results as exhibited by the lactation curve would be the same by the theory of Ragsdale, Turner, and the writer, as by the theory of Gaines and Davidson, so that it would not be profitable to discuss the matter further in the absence of substantiating experimental evidence.

## VII. APPENDIX

The general ideas presented in the preceding section suggest certain corollaries, and it is the purpose of the present section to bring them together.

One of these, a theoretical idea, relates to limits. This may be illustrated by examples taken from the data.

**a. The Limit of Egg Production in the Domestic Fowl.**—In a preceding section we have shown that the time rate of ovulation in the domestic fowl (as represented by a given group of birds under observation) begins at the rate of 172 eggs per year, and that this time rate of egg production declines with increasing age at the rate of 12.3 per cent per year. In brief, the course of ovulation in these birds would be represented by the equation

$$E = 172e^{-0.123t}$$

in which  $E$  is the number of eggs laid per year at the age  $t$ . Data are available up to 8 years. From this equation it is possible to compute the number of eggs that the average bird (of this group) could lay at any other age. There is no practical need for making such computations, because poultrymen do not usually keep chickens after the age of 8 years. The interest for such prediction is only of a theoretical kind. There is also a theoretical interest in computing the total number of eggs that a bird could produce if she were to live indefinitely. What, then, is the theoretical *limit* of egg production?

To answer this question it is only necessary to integrate the above equation between the limits of  $\frac{1}{2}$  year (the age when egg laying begins) and infinity.

The following are the steps in the integration:

$$E = \int_{\frac{1}{2}}^{\infty} Ae^{-kt} dt = \frac{A}{-k} \left[ e^{-kt} \right]_{\frac{1}{2}}^{\infty} = \frac{179.2}{0.123} e^{-\frac{0.123}{2}} = 1370$$

In other words, if egg laying were to continue indefinitely the total number of eggs laid by the average fowl of the group would be 1370 eggs. This number of eggs, it may be noted, is less than the number of oocytes that are contained in the chicken. Thus, Curtis (*cf.* Maine Agr. Exp. Sta. Bul. 205, 1912) found an average (in thirteen hens) of 1814 oocytes visible to the naked eye. Since there must be many more eggs not so visible, it appears that it is not the number of oocytes in the hen that limits the course of egg production, but rather the decline in vigor of some limiting organ or organs (*cf.* Brody, Henderson, and Kempster, *J. Gen. Physiol.*, 1923, VI, 41).

b. **The Limit of Milk Production in the Dairy Cow for a Lactation Period and for a Life Cycle.**—The integration of equation (2), that is of

$$W = Ae^{-kt}$$

between the limits of zero and infinity yields the result  $\frac{A}{k}$ . Since this

equation (practically) represents the course of decline of milk yield with the advance of lactation ( $A$  is the *theoretical* maximum production at parturition and  $k$  is the relative decline in milk yield), therefore the limiting value for milk production for a lactation period can be easily found. In the case of the farrow group of cows (*cf.* Fig. 10) we have found  $k = .055$ ;  $A = 1170$  pounds per month. Therefore the limiting milk yield for a lactation period is  $\frac{1170}{.055} = 21,300$  pounds—which is only a little

over twice the milk yield for the first year (about 10,000 pounds).

The same procedure may be used for estimating the limit of milk production of a cow with respect to age. From Fig. 9, following 10 years, the milk yield declines at about 4 per cent per year. At 10 years the fat production was approximately 535 pounds per year. Therefore following 10 years the limiting value of butterfat production (if the cows lived indefinitely) is  $\frac{535}{.04} = 13375$  pounds. Up to 10 years

the average production of the same cows was 4316 pounds. In other words, preceding 10 years, the butterfat produced is about one-fourth of the limiting amount following 10 years.

c. **The Relation Between the Maximum Milk Production in a Lactation Period, the Relative Rate of Decline with the Advance of the Period of Lactation, and the Total Milk Production in a Lactation Period.**

—The total milk produced during a lactation period is obviously dependent on two factors: (1) The maximum milk yield with which lactation begins ( $A$  in equation 2), and the rate of decline from this maximum with the advance in the period of lactation ( $k$  in equation 2). Students of inheritance of milk production are at present actively engaged in investigating the inheritance of these two characters ( $A$  and  $k$ ) and it is for this reason desirable to know the quantitative relations between the two variables. It is particularly desirable to have a simple method for computing the value of persistency,  $(1-k)$ .

A historical discussion of this problem is given by Gaines (J. Agric. Research, 1927, XXXIV, 373). For the present it will be sufficient to say that C. W. Turner (J. Dairy Sci., 1926, IX, 203), and apparently

H. G. Sanders (J. Agric. Sci., 1923, XIII, 169), have proposed the ratio of the milk yield for the lactation period to the maximum production, as a measure of the persistency. What we wish to do is to eliminate

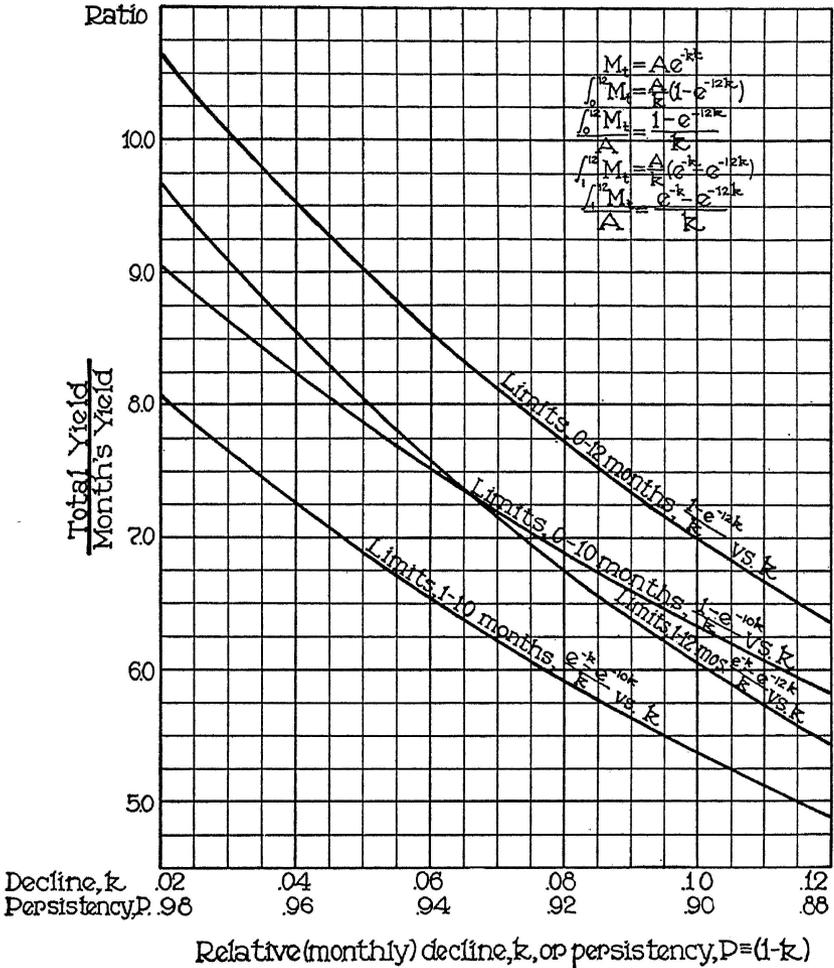


Fig. 20.—These curves indicate the relation between the fractional (or when multiplied by 100, percentage) decline in milk yield with the advance of the period of lactation and the total production (for 10 or 12 months) when the maximum yield is known. (For other explanations see text. For practical applications see C. W. Turner, J. Dairy Sc., 1926, IX, 203; also W. L. Gaines, J. Agric. Research, 1927, 34, 373 and Univ. Illinois, Agric. Expt. Station Bul. 288, 1927).

certain theoretical (not necessarily practical) errors in their methods of computations, and to indicate a train of reasoning for deriving the relation of the relative decline ( $k$ ), or of the relative persistency ( $1 - k$ ),

from the values of yield for a lactation period of a given length and from the maximum yield.

The expression relating milk yield,  $M_t$ , with time,  $t$ , after calving, and with the theoretical maximum milk yield,  $A$ , was already shown to be

$$M_t = Ae^{-kt}$$

The total theoretical production for 12 months (which is the usual duration of a lactation period) may be obtained by integrating this equation between the limits of 0 and 12

$$\int_0^{12} M_t = -\frac{A}{k}e^{-kt} \Big|_0^{12} = \frac{A}{k}e^{-12k} - \frac{A}{k} = \frac{A}{k}(1 - e^{-12k})$$

Dividing both sides by the maximum production,  $A$ , we obtain

$$\frac{\int_0^{12} M_t}{A} = \frac{1 - e^{-12k}}{k}$$

The term on the left gives the ratio of the production for the year to the maximum production for the month (i. e., to  $A$ ). We may next prepare a chart in which the ratio of the total production  $\int_0^{12} M_t$  to the maximum production ( $A$ ) are plotted against  $k$ , as is shown in Fig. 20.

Having this chart, it is easy to interpolate the value of the relative decline ( $k$ ) or the persistency ( $1 - k$ ) of milk secretion whenever the total production and the maximum production are known.

Since the first month's production is not definitely known, we may prepare a chart in which the ratios of production between the end of the first month and the end of the 12th month to the maximum yield are plotted against  $k$ .

$$\int_1^{12} M_t = \frac{A}{k}e^{-kt} \Big|_1^{12} = \frac{A}{k}e^{-12k} - \frac{A}{k}e^{-k} = \frac{A}{k}(e^{-12k} - e^{-k})$$

Dividing both sides by  $A$  we obtain

$$\frac{\int_1^{12} M_t}{A} = \frac{e^{-12k} - e^{-k}}{k}$$

Similarly ratios for any other interval of time may be plotted against  $k$  as shown in Fig. 20 and the values of  $k$  may then be interpolated from the resulting curves.

It is perhaps needless to add that if the time rates for milk yield for each of two months are known, then the relative rate of decline may be determined by subtracting the natural logarithms of the milk

yields. Thus if the milk yield for any one month is 994 pounds and for the following month it is 942 pounds, then the rate of decline is  $6.902 - 6.848 = .054$  or 5.4 per cent per month. The persistency of milk yield is  $1.000 - .54 = .946$  or 94.6 per cent per month. The milk yields need not be for successive months. This if during the third month of the lactation period the milk yield is 994 pounds and during the twelfth month it is 613 pounds, then the difference between the natural logarithms of the two numbers is  $6.902 - 6.418 = .484$ . This difference is then divided by the time interval between the two yields, namely  $12 - 3 = 9$  months, resulting in a relative decline of  $\frac{.484}{9} = .054$  or 5.4

per cent per month, as before. Of course, it is not safe to compute the value of a constant on the basis of only two values, as the third and twelfth months, on account of the probable experimental error in one or the other value. Evaluating the constant by the interpolation chart (Fig. 20) is for this reason a safer procedure. Gaines (Illinois Agr. Exp. Sta. Bul. 288, 1927) suggests the use of the methods of least square and also an ingenious mechanical device for evaluating the constant of decline in milk secretion with the advance of the stage of lactation. Both of the methods of Gaines, however, are based on our equation (2).

**d. Equivalence Charts Between Growth in Weight and Increase in Milk Yield.**—Since, as previously shown, milk yield and body weight follow approximately the same course until the age of the animals is 9 years, it is possible to prepare equivalence charts for the two processes by the method explained in Res. Bul. 102 of this series.

The charts, when taken with their legends, are self-explanatory. The charts in this section are divided into six series as follows:

*Series A.*—Increase in body weight and in milk yield, presented in the form of equivalence charts (Figs. 21a to 21c).

*Series B.*—The increase in milk yield with advancing age in cows on test and cows not on test. The milk yields, in terms of percentage of maximum yield, are plotted against a common age axis (Figs. 22a-c).

*Series C.*—Equivalence charts between the curves of Register of Merit Jersey Cows in 1914-1921 group; 1922 group; and 1923 group (Fig. 23a and 23b).

*Series D.*—Equivalence chart for Advanced Registry records of Ayrshire, Guernsey, Holstein, Jersey, and Shorthorn cows (Fig. 24).

*Series E.*—Equivalence charts for curves of the *same* breeds of cows but under different conditions of management (Fig. 25a-e).

*Series F.*—Equivalence between growth in weight, increase in milk yield and in twinning with age (Fig. 26).

In many cases the curves, and the corresponding age axes, are numbered. The numbers refer to the columns of Table 11, Dairy Section of

Res. Bul. 96 of this series from which the data were plotted. The values of the constants ( $A$ ,  $k$ ,  $t^*$ ) for the various groups of data are given and numbered in the same sequence in Table I of the present bulletin.

The following general conclusions may be made on the basis of these charts.

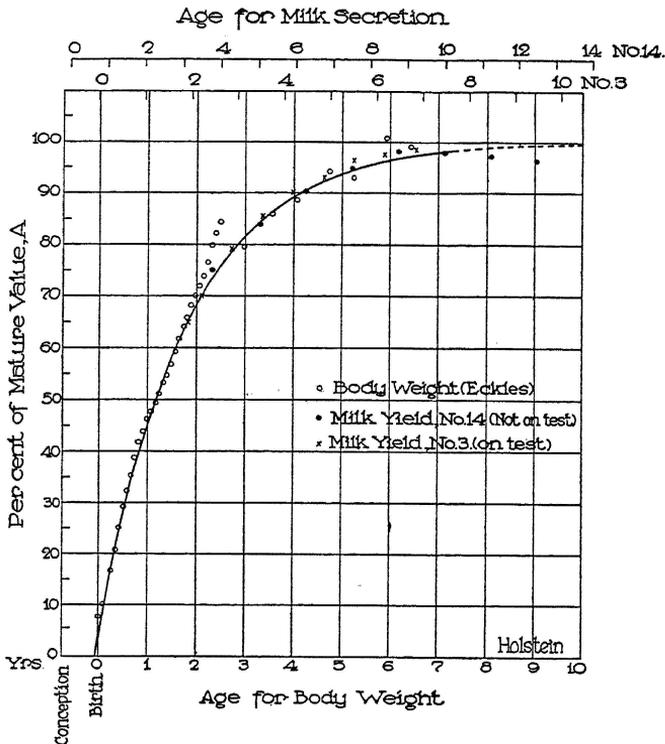


Fig. 21a.—Growth equivalence for body weight and for milk yield, Holstein cattle. The weight data were obtained on animals owned by this (Dairy) Department and given in detail in Res. Bul. 96 of this series. The data for milk yield are likewise given in Res. Bul. 96 of this series. The numbers along the axes (No. 3, No. 14, etc.) refer to the number of the column in the table on milk secretion given in Res. Bul. 96 and also in Table I of this bulletin. See Res. Bul. 102 of this series for the method of preparing equivalence charts.

The maximum milk yield is reached at earlier ages for animals on test than for those not on test. This is probably attributable to the better diet these animals receive. It is well known that the nature of the diet exerts a profound influence on the speed of approach to the mature weight and, consequently, probably also on the speed of approach to the mature milk yield (*cf.* Osborne and Mendel, *J. Biol. Chem.*, 1926, LXIX, 661).



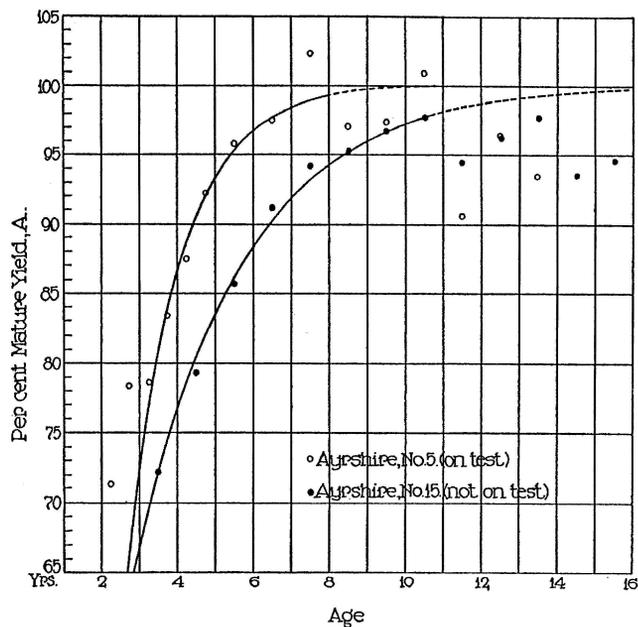


Fig. 22a.—A comparison of the age curves of milk yield of cows on test and of cows not on test. The milk yields are given in terms of percentages of the maximum (*A*) values. Ayrshire cattle. Note that cows on test not only have a higher mature milk yield, but they also reach the maximum at an earlier age.

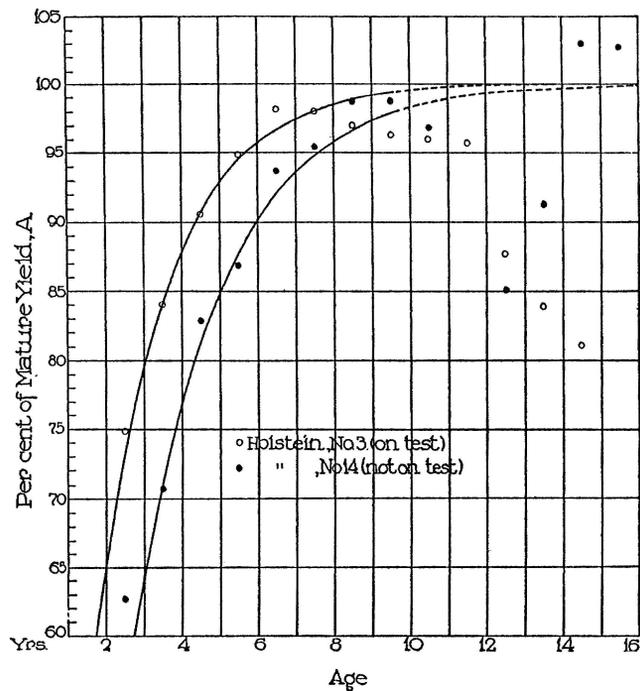


Fig. 22b.—A comparison of the age curves of milk yield of cows on test and of cows not on test. Holstein cattle.

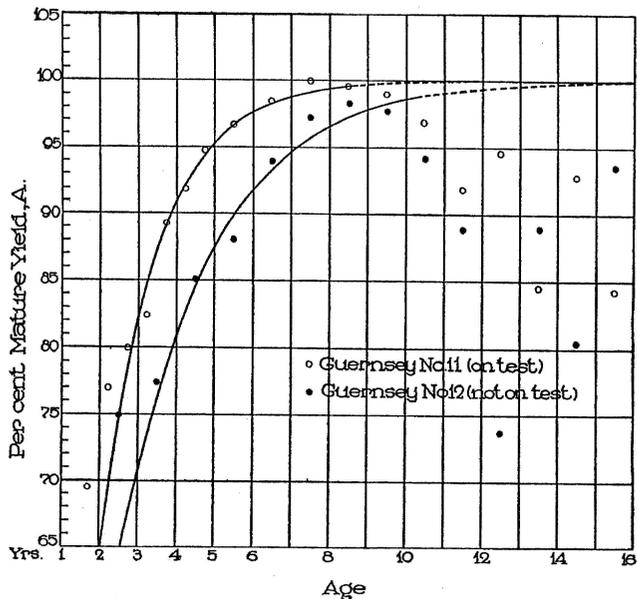


Fig. 22c.—A comparison of the age curves of milk yield of cows on test and of cows not on test. Guernsey cattle.

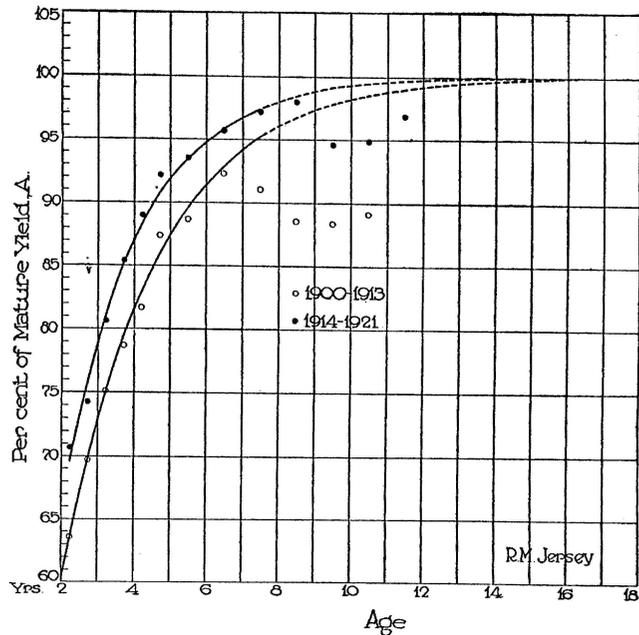


Fig. 23a.—A comparison of the age curves of milk yield of R. M. Jersey cattle during the years between 1900-1913; and 1914-1921. Note that in the later period the cows not only reached a higher mature yield, but they also reached maximum production at an earlier age.

Of course, it may well be, as Graves and Fohrman suggest, that animals on test undergo additional development because they are on test (on account of more frequent and thorough milking, or is it because the test is repeated on account of the confidence that the dairyman places in the animal, or is the animal's better performance on second test an expression of the dairyman's increased experience in getting the best from the animal?).<sup>1</sup> It is also conceivable that high milking qualities and early maturity are correlated.

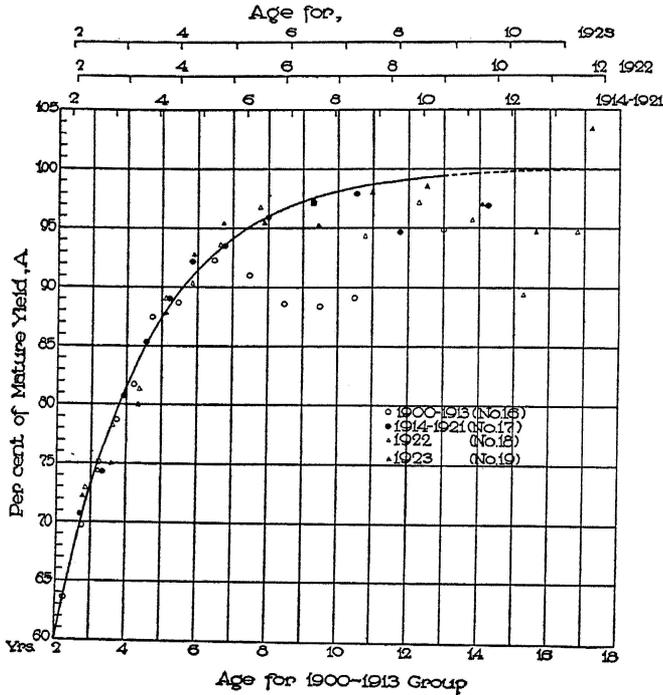


Fig. 23b.—Equivalence chart for Jersey records obtained during various periods.

The important new *fact* not known to dairymen and which is clearly brought out by the present analysis, is that the average cow on test reaches her maximum production earlier than the average cow not on test. This will be of particular interest to the student of inheritance of milk secretion who has occasion to use "conversion factors" to correct for age. Apparently the conversion factors obtained on one set of animals (or on animals under one set of conditions) are not necessarily applicable for other sets of animals (or for animals under a different set of conditions).

Another conclusion brought out by the present analysis is that maximum milk yield is apparently attained at a somewhat later age than maximum body weight. This difference with regard to maxima, may however, be due to the statistical treatment of the data. Thus

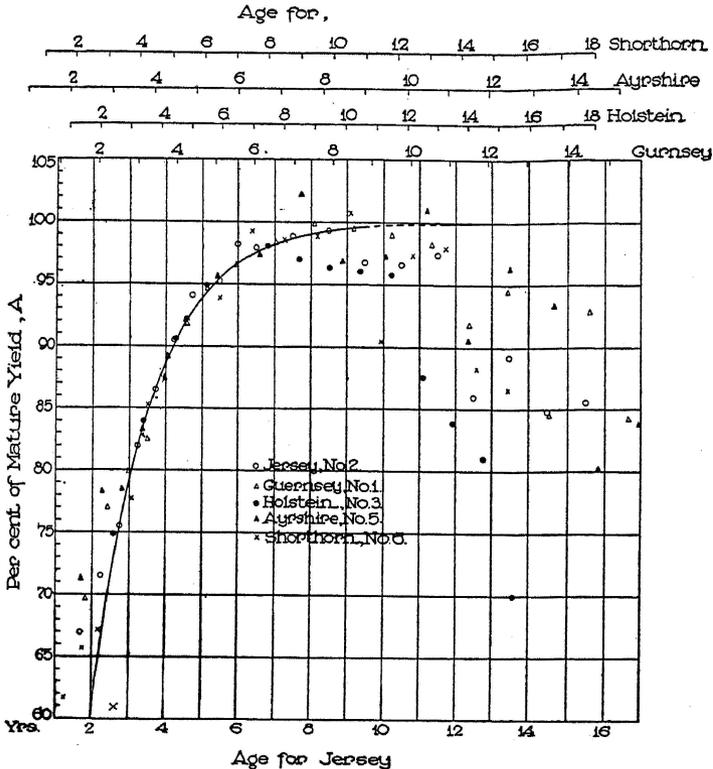


Fig. 24.—Equivalence chart for Advanced Registry records of milk yields for five breeds of dairy cattle. The equivalence referred to applies only, of course, for the period preceding 9 years. Following 9 years there is an evident tendency for the milk yields to decline in spite of the fact that the population becomes increasingly selective. The numerals refer to the group of cows in Table I and to the corresponding column in the table on milk yields in Res. Bul. 96 of this series.

the weights for the R. M. Jersey cows are usually reported at the end of the lactation period, whereas the milk yields are referred to the age at the beginning of the lactation period. We have no data for growth in body weight and increase in milk secretion for the same animals recorded at exactly the same ages.

e. **The Relation Between Milk Yield, Butter-Fat Yield and Butter-Fat Percentage in Milk.**—In some of the charts on age changes in milk secretion we have plotted milk yield against age, and in others butterfat yield against age. The interchangeable use of milk and of butter-

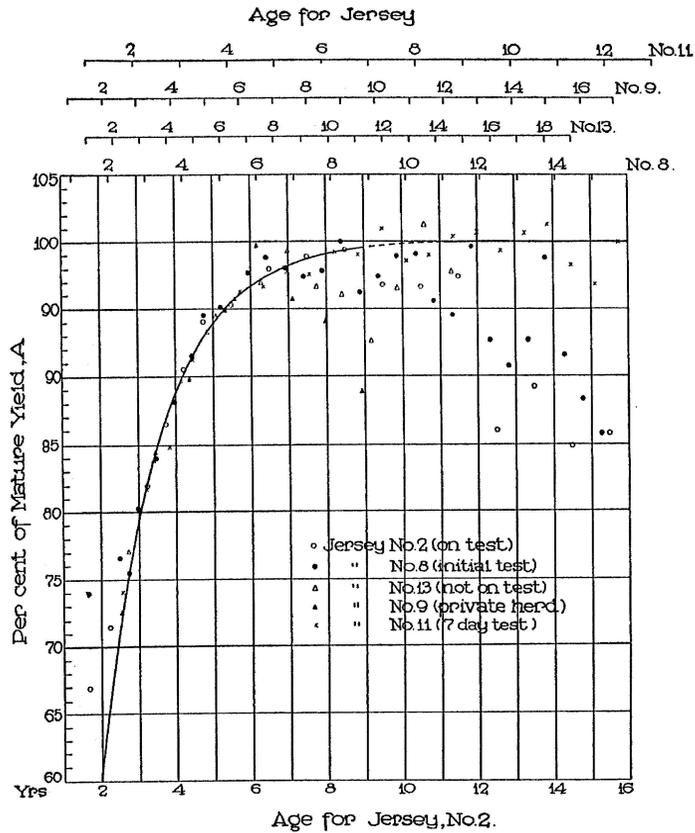


Fig. 25a.—Equivalence chart for age curves of milk yield of the same breed (Jersey) of cattle, but under different conditions of management. Note that No. 11 (on 7-day test) requires the least time to reach the maximum performance. Then come Nos. 2 and 8 (on test), No. 13, the group not on test, reaches its maximum last of all.

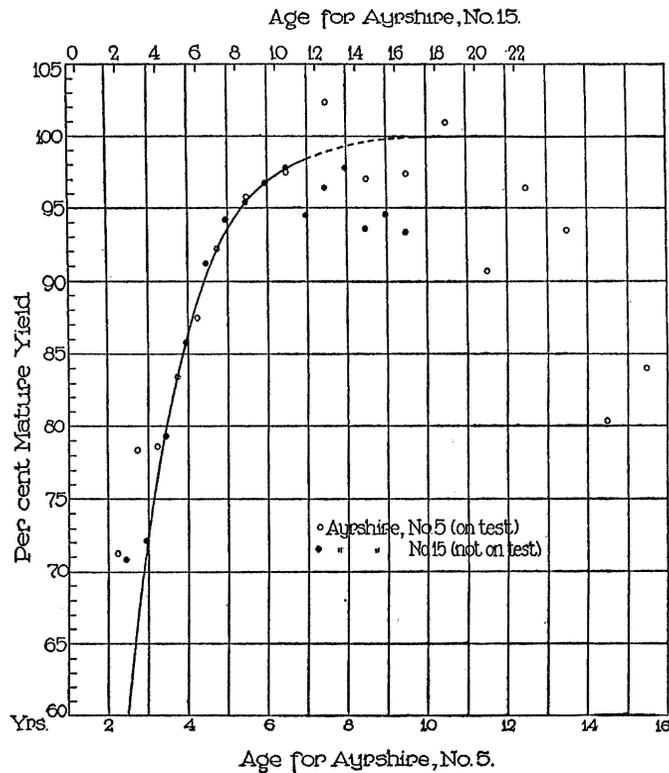


Fig. 25b.—Equivalence chart for Ayrshire records obtained under test and under non-test conditions.

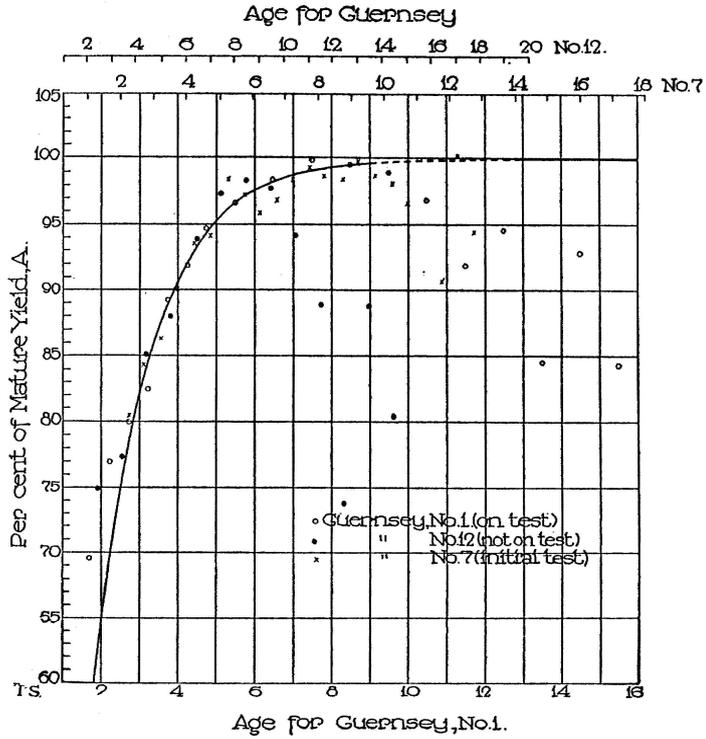


Fig. 25c.—Equivalence chart for Guernsey records.

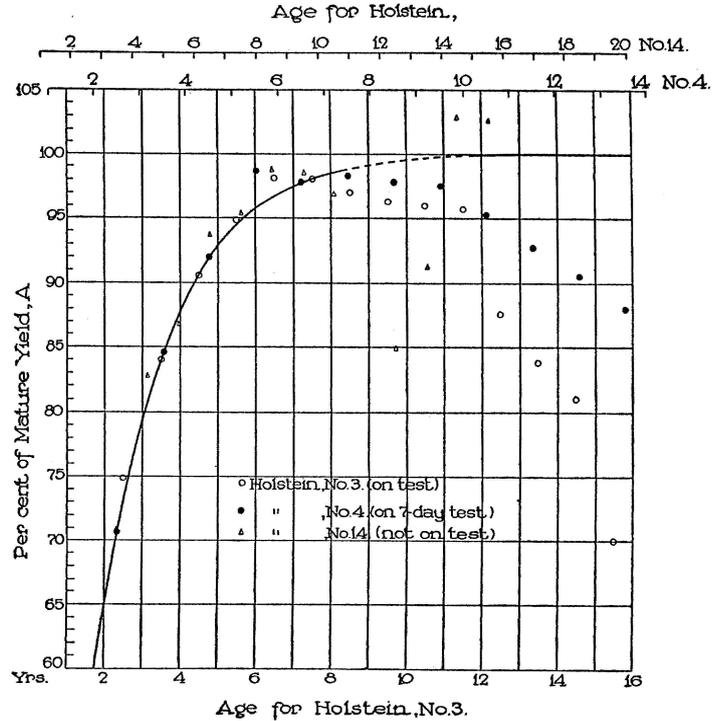


Fig. 25d.—Equivalence chart for Holstein records.

fat as indices of age changes in mammary activity may be justified on the ground that for a given group of cows the percentage of fat in the milk remains constant within the limits of errors of the present computations, and the fat yield may be taken as an index of the milk yield.

If, however, the individuals of a population are classified according to the fat percentage of their milk, then it is found that, on the average, the higher the milk yield, the lower the percentage of fat. In other words,

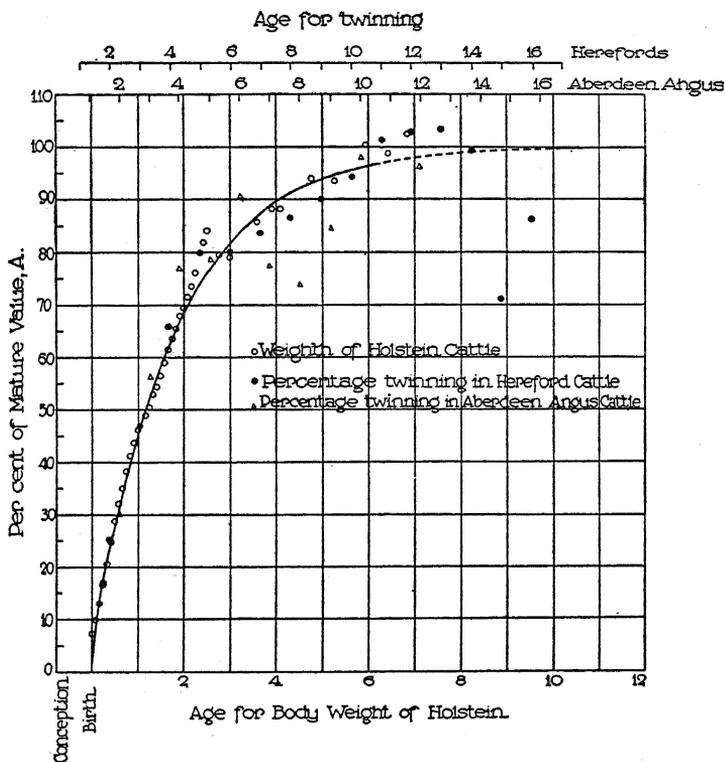


Fig. 26.—Equivalence between growth in weight and increase in twinning with age. The weights refer to the Missouri data (Res. Bul. 96). The twinning refers to data by Jones and Rouse. It appears that the two sets of data follow the same course.

when other conditions remain the same, and animal A yields double the milk of animal B, the butterfat yield of A is probably less than double the butterfat yield of B. It appears that the butterfat secreting mechanism is quantitatively more or less independent of the milk secreting mechanism and that it tends to be more constant than the milk yield. A given change in milk yield is accompanied by a relatively lesser change in butterfat yield. The relation between butterfat and milk yield is somewhat analogous to the relation between the volume

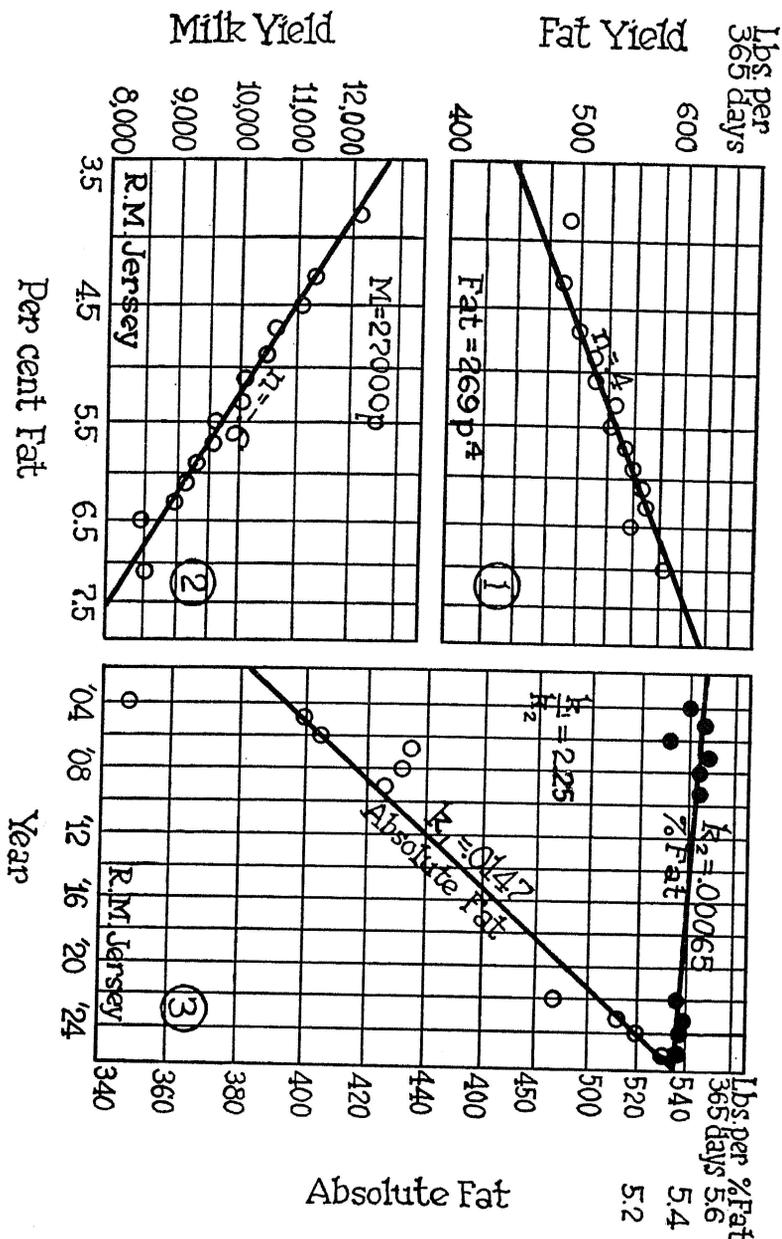


Fig. 27.—Curve (1) shows that in the given R. M. group of Jersey cattle the absolute butter-fat production tends to vary as the 0.4 power of the percentage of fat. Curve (2) shows that milk yield tends to vary inversely as the .6 power of its butter-fat percentage; or to put it in more logical form, the butter-fat percentage tends to decrease with increasing milk yield and on the average the butterfat percentage tends to vary inversely with the 1.7 power of the milk yield. Curve (3) shows the *relative* increases in butterfat yield and in percentage of fat of the milk from 1904 to 1925 (in R. M. Jersey Cattle). The percentage of fat has been decreasing while the milk yields have been increasing. The rising butterfat production from 1904 until 1925 is therefore due not to increasing butterfat percentage of the milk, but to increasing milk yields. Indeed, the butterfat percentage is seen to decline (the rise in milk yield is 22.5 times as great as the decline in butterfat percentage). Turn page on side to read curves.

of urine and the urine solids excretion. A change in the time rate of urine output is not accompanied by a proportionate change in the time rate of excretion of the urine constituents.

Assuming that milk yield tends to vary in an inverse direction with the percentage of its fat, then it might be possible to represent this relationship by the equation

$$M = Cp^{-n} = \frac{C}{p^n} \quad (4)$$

in which  $M$  is the milk yield of percentage of fat  $p$ . The exponent  $n$  would, of course, be unity if milk yield varied inversely with the percentage of its fat, and  $C$  would represent the absolute fat production. In other words, if  $n$  were unity, the total fat production would remain constant

$$Mp = C = \text{Fat production}$$

But it is well known that the butterfat yield is not constant, varying both with the percentage fat and with the milk yield. It follows, therefore, that  $n$  is not unity.  $n$  is some proper fraction.

Assuming that equation (4) represents the relation between milk and its fat percentage, then we may determine the value of  $n$  by taking logarithms of both sides of equation (4)

$$\log M = \log C - n \log p$$

and plotting  $\log M$  against  $\log p$ ; or plotting  $M$ , milk yield, against  $p$ , percentage of fat, on logarithmic coordinate paper and determining the slope of the resulting curve. This is done in Fig. 27 for Register of Merit Jersey cows, employing the data recently published by the Jersey Cattle Club (*cf.* Lynn Copeland, *J. Dairy Sci.*, 1927, 10, 344). The value of  $P$  is of the order of 0.6. That is, for this group of cows the milk yield tends to vary inversely as the 0.6 power of the percentage of fat. The same chart shows that the absolute fat yield tends to vary, not directly with the percentage of fat but only with the 0.4 power of the percentage of fat. Similar relations between milk yield, butterfat yield and percentage of fat may, presumably, be determined for other breeds of cattle.

It should be noted before closing that Gaines and Davidson (*Univ. Ill. Agr. Exp. Sta. Bul.* 245, 1923) found the equation

$$M = \frac{a}{2.66 + t} \quad (5)$$

to represent the relation between milk yield,  $M$ , (in pounds) and fat percentage,  $t$ . The term  $A$  is a constant determined by the productive level of the particular group of animals. These authors propose that the milk yield of cows should be corrected to the physiological equivalent of 4.0 per cent (fat) milk by the equation  $FCM = 4M + 15F$  in which  $FCM$  is "fat corrected milk",  $M$  is the actual milk yield, and  $F$  is the actual fat yield (all in pounds).

#### f. Historical Notes Relating to the Mechanism of Milk Secretion.

—Since equations (1), (2), and (3) used to represent the kinetics of milk secretion have the same form as the equations representing the kinetics of certain physico-chemical processes, the suggestion presents itself that the kinetics of milk secretion might ultimately be limited by some physico-chemical process. This suggestion is not as preposterous as it may seem in view of the fact that the process of milk secretion is, after all, physico-chemical in nature. The following notes have some bearing on the relative importance of the nervous system and of certain chemical substances, catalyzers or hormones, on the process of milk secretion.

The activity of the mammary gland is, perhaps under normal condition, not dependent on nervous control but rather on the influence of hormones as indicated by the following facts: When twins have a common circulation but separate nervous systems, and one twin becomes pregnant, the mammary glands of both develop, and after delivery both produce milk (*cf.* the case of Rosa and Josepha Blazek, in *Deut. Med. Wochensch.* 1910, XXXVI, 987, and *British Med. J.*, May 23, 1910). Indeed Ribbert transplanted a mammary gland (in the guinea pig) to the neighborhood of the ear thus severing all its nervous connections. In a subsequent pregnancy this gland enlarged as usual, and milk could be obtained from it (*Arch. Entwicklmech. Organ.* 1898, VII, 688). Golz and Ewald observed that the mammary glands in the pregnant bitch developed normally after removal of the lumbo-sacral cord (by severing all connections between the pelvic organs and the mammary gland. *cf.* *Arch. Ges. Physiol.*, 1896, LXIII, 362).

Several positive investigations support the idea that the development and activity of the mammary apparatus is dependent on certain catalyzers produced by the fertilized ovum. Lane-Clayton and Starling found that the mammary glands of a virgin rabbit developed, and in the case of a multiparous rabbit the gland secreted milk, by injections of extracts of fetus (*Proc. Roy. Soc. London, B*, 1906, LXXVII). A good deal of work is recorded on the influence of extracts of corpus luteum hypophysis, placenta, involuting uterus, lactating gland, on milk secretion (*cf.*, among others, O'Donoghue, *Quart. J. Microscop. Sci.*, 1912, LVII; Ott and Scott, *Proc. Soc. Exp. Biol. and Med.*, 1910, VIII, 48 and 49; Lederer and Przibram, *Arch. Ges. Physiol.*, 1910, CXXXIV; Schafer and Mackenzie, *Proc. Roy. Soc., London*, 1911, B, LXXXIV; Mackenzie *Quart. J. Exp. Physiol.*, 1911, IV). Allen and his co-workers believe that the placenta has an endocrine function in initiating growth of the mammary glands during gestation (*J. Am. Med. Ass'n.*, 1925, LXXXV). Meyer found that the growth of the mammary gland (in the rat) during puberty is correlated with the development of graafian follicles (*Am. J. Anat.*, 1916). The cyclic uterine changes in the guinea pig were found to be accompanied by changes in the mammary gland (Loeb and Hesselberg, *J. Exp. Med.*, 1917). This review indicates that the development of the mammary gland is initiated by a hormonal mechanism from the pregnant uterus.

Following the maximum development, the activity of the mammary gland declines, presumably on account of a species of senescence and possibly death of the secreting cell; or the secreting cells are inactivated in somewhat the same manner as bacterial cells are inactivated under unfavorable conditions. The significance of the logarithmic course of inactivation of bacterial cells with time is at present a debated question (*cf.* *Chick. J. Hyg.*, 1908, VII, 92; 1910, X, 237; Yule, *Royal Statis. Soc.*, 1910, LXXIII, 26; Loeb and Northrop, *J. Biol. Chem.*, 1917, XXXII, 103; Brooks, *J. Gen. Physiol.*, 1918, I, 61; Smith, *Ann. Appl. Biol.*, 1921, VIII, 27), and a definite conclusion has yet to be formulated.

TABLE 1.—VALUES OF CONSTANTS *A*, *k*, *t*\*, ETC., FOR VARIOUS GROUPS OF DATA

No. Breed and condition of test	<i>A</i> Theoretical yield at Maturity		<i>B</i> Computed on basis of concept. age	100 <i>k</i> Theoretical % of monthly de- cline in milk or fat yield	Age from birth at			
					<i>t</i> *	½ mature value	¾ mature value	98% mature value
	<i>kg.</i>	<i>lbs.</i>	<i>kg.</i>	<i>per cent</i>	<i>mos.</i>	<i>yrs.</i>	<i>yrs.</i>	<i>yrs.</i>
1. Guernsey on official test. Yield of butterfat per yr.	240	529	550	5.6	14.8	2.5	6.3	7.3
2. Jersey on official test. Yield of butterfat per yr. ---	239	527	530	5.2	15.5	2.7	6.8	7.9
3. Holstein-Friesian on official test. Yield of butterfat per year.-----	308	679	470	4.4	9.6	2.6	7.9	8.7
4. Holstein-Friesian on official test. Yield of butterfat during a 7-day test.-----	8.0	17.6	19.9	5.6	16.9	2.6	6.4	7.4
6. Ayrshire on official test. Yield of butterfat per yr. .	212	467	900	6.0	24.0	3.1	6.6	7.6
7. Shorthorn on official test. Yield of butterfat per yr.	185	408	456	4.6	19.6	3.4	7.9	9.2
8. Guernsey on official test for <i>first time</i> . Yield of but- terfat per year. "Single letter" class.-----	228	503	290	4.8	5.0	2.1	6.4	7.6
9. Jersey on official test for <i>first time</i> . Yield of butter- fat per year -----	218	481	400	5.1	12.0	2.5	6.6	7.7
10. Jersey in one herd Yield of milk for 1st 8 months .	2520	556	4400	4.7	12.0	2.7	7.1	8.4
11. Jersey in a private herd of same 88 cows completing 5 milking yrs. Yield of milk during 1st 8 months after calving.-----	2625	5787	8800	6.0	20.2	2.9	6.3	7.3
12. Jersey on test. Yield of milk during 7-day tests.---	253	558	495	6.5	10.3	1.9	5.1	6.0
13. Guernsey not on test, milked only twice a day. Yield of milk per year.-----	2930	6460	4500	3.6	12.0	3.4	9.3	10.9
14. Jersey not on test, milked only twice per day. Yield of milk per year.-----	2700	2952	2850	3.7	1.5	2.8	8.2	9.7
15. Holstein-Friesian not on test, milked only twice a day. Yield of milk per yr.-----	5100	11244	9400	3.6	17.0	3.8	9.2	11.3
17. Ayrshire yield of milk during 7-day interval.-----	90	198	118	3.0	9.0	3.8	10.8	12.8
18. Jersey cattle on official test 1900-1913 groups. Yield of butterfat per year.-----	550	1213	641	3.2	4.8	3.2	9.8	11.6
19. Jersey cattle on test 1914-21 groups. Yield of but- terfat per year.-----	540	1190	705	4.0	6.7	2.7	7.7	9.4
20. Jersey cattle on test 1922 group. Yield of butterfat per year.-----	570	1257	934	4.8	10.3	2.5	6.9	8.1
21. Jersey cattle on test 1923 group. Yield of butterfat per year.-----	600	1323	1100	5.0	12.1	2.5	6.7	7.9