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Growth and Aging Problems in Agriculture

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AGRICULTURE IS BASED on the phenomena of growth and development. The aims and attitudes of academic agriculturists, however, differ somewhat from those of academic biologists. For instance, the agriculturist must work for predetermined objectives which are essentially to grow or to produce bigger and better agricultural crops of plants, animals, and such of their products as eggs, milk, wool, and muscular work. The only crop that academic biologists are expected to produce is good "papers," with no limitation on objectives.

The agriculturist, moreover, has to contend with a thousand uncontrollable or uncontrolled factors—reproductive, hereditary, nutritional, climatic and ecological, engineering, social-economic, and so on—which influence his productive objectives.

Then, too, the agricultural investigator has to solve special financial and methodological problems not encountered by the academic biologist. For instance, the financial costs and experimental methods of investigating a cow with its fabulous stomachs and huge consumption of roughage are of a very different order than those of investigating a rat with a simple stomach or an *obelia* in sea water. Likewise, the problem of investigating large and densely populated fields of plants subject to the vagaries of weather, insects, infections, and other pests is of a different order than that of investigating a few plants under the controlled conditions of a greenhouse laboratory.

Specific Growth Problems

It is important to remember that the agriculturist defines "growth" not as "developmental biosynthesis" but as the production of beef steaks and pork chops, milk and eggs, beans and potatoes, peaches and tomatoes, wool and cotton, flowers, race horses, Easter rabbits, Christmas trees, and so on.

The usual market (slaughter) weight of pigs is 225 pounds. The unimproved pig may require 12 months to attain this weight at a feed cost of, perhaps, 800 pounds per 100 pounds gain in body weight. But some pigs may attain this weight in 6 months at a feed cost of but 400 pounds per 100 pounds gain. Moreover, the flesh of the rapidly growing animal is more tender than that of the slowly growing one.

A major problem in agriculture is to develop such rapidly and efficiently growing animals that transmit consistently these desirable characteristics to their progeny. Unfortunately, only a few of the rapidly growing pigs produce rapidly growing progeny, and these few can be detected by progeny tests alone. But by the time adequate progeny tests are completed, the original stock is usually no longer available or has become infertile or impotent. This calls attention to the aging problem, the importance of learning how to delay it and how to utilize fully proved, aged animals, especially for reproductive purposes. To overcome some of the difficulties of utilizing fully the few desirable progeny-tested animals, agriculturists developed satisfactory methods for artificial insemination. This enables the utilization of one sire for 50 to 100 times as many females as by the natural method. A single ejaculate, for example, may provide, if necessary, enough semen for 300 cows (Salisbury), and 500 cows can easily be bred to one bull per month by artificial insemination. Over 250,000 dairy cows in the United States were bred this way in 1945. Old animals may, perhaps, be "rejuvenated" temporarily by certain hormones and/or other catalysts and by nutrients. The involved ideas are not new in agriculture, folklore, or fiction, but their wide practical application is new. And the agriculturist—especially in Missouri—usually believes that knowledge is of value only in so far as it is applied for productive purposes.

Here is an agriculturally practical example of "rejuvenation." About 1924 F. A. E. Crew reported dramatically that he "rejuvenated aged fowls (5 to 8 years) through thyroid medication." The "birds became rejuvenated, looking fresh . . . quickly started to produce eggs at a faster rate." Only recently, however, has C. W. Turner, of the Missouri Station, ap-

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plied this medication on a large scale to fowls, confirming Crew's observation. Five-year-old birds fed thyroactive protein produced approximately 30 per cent more eggs than control birds. Berliner and Warbritton, and Bogart and Mayer, of the Missouri Station, also reported favorable results of thyroxine administration on the fertility of old rams and on fertility during the period of "summer sterility" associated with hot weather.

Another example is the rejuvenating effect of topical applications of estrogens on senile genital mucous membranes and even on skin (M. A. Goldziehr, 1946). C. W. Turner is administering estrogens to fowls in the attempt to prevent the deterioration of their oviducts at the end of the laying season.

Returning to the problems of rate and efficiency of growth, what was said about growth-rate differences in pigs holds true for other farm animals and their products, as illustrated by the following examples.

The usual market (slaughter) weight of beef steers is 900 pounds. Unimproved cattle may attain this weight in two years at a feed cost of perhaps 800 pounds TDN per 100 pounds live weight, whereas many individual animals attain it in one year at a feed cost of perhaps 400 pounds TDN per 100 pounds live weight. Moreover, as in pigs, the flesh of the rapidly growing animals is more tender. Here again, but few individuals transmit their rapid-growth characters consistently, and these rare individuals can at present be found by progeny tests alone. By the time the progeny tests are completed the original animals are likely to be unavailable.

An unimproved cow may produce perhaps 1,000 pounds of milk per year, but there are cows producing 42,000 pounds (average of 115 pounds a day). Although such cows are rare, they demonstrate the potentialities of cattle, in that 40 or 50 quarts of milk may be produced where one quart was produced previously.[1]

An unimproved fowl may lay some 30 eggs a year beginning at 1 year of age. On the other hand, there are rare chickens that begin laying at 5½ months of age and produce 360 eggs the first year.[2] These birds demonstrate the plasticity and productive range of farm animals and the possibility of producing a dozen eggs where one was produced before.

The most publicized although less dramatic increase was achieved in corn production by utilizing mostly the phenomenon of the so-called hybrid vigor, especially with regard to resistance to unfavorable temperatures and to disease. The range of increase in yield by the use of hybrid seed varies with climatic and soil conditions. The average increase in production is only 25 per cent, but the absolute increase on a $3,000,000,000 crop is huge. Greater yield, earlier maturity, and resistance to diseases (wilt, mildew, smut, smudge, blotch, etc.) were obtained in many plants by similar breeding.

Among animals, the phenomenon of hybrid vigor is best known in the mule, superior to either mare or jackass for hard labor in hot climates. Resistance to heat is also shown in crosses between certain breeds of European beef cattle (Aberdeen Angus) and Indian cattle (Guzerat, Brahman), and also in crosses with African cattle (Africander). Moreover, the weaning age, meat tenderness, and dressing percentages appear to be higher in the crosses. Resistance to cold and to infections may perhaps be developed similarly by appropriate breeding.

Attempts are being made to utilize this phenomenon of hybrid vigor in the breeding of dairy cattle and poultry. Crosses of Jersey and West Indies cattle are said to be more resistant to heat than the pure Jersey. Crosses between European breeds, such as Red Danish and Jerseys, Holsteins, or Guernseys, are said to give satisfactory results (O. E. Reed). Purebred breeders, however, object strenuously to crossbreeding.

Individual differences in rates of growth and fattening are common in many species, including mice and men. Physicians attribute them in man to differences in food consumption in relation to muscular activity. This is a thermodynamically reasonable inference. But what causes differences in food consumption in relation to muscular activity?

There is a strain of mice that shows an unusual tendency to rapid fattening. This is attributed to a certain "yellow gene." But how does this gene accelerate fattening? An insight into this situation might perhaps be furnished by energy balance experiments and by assays of hormones and other suspected catalysts and nutrients as already noted.

The agriculturist usually conducts investigations not on the ultimate component factors but on complexes such as the complex "growth rate," "milk production," "egg production," "wool production," "racing ability," or "work ability" (in horses or mules), and so on. Maybe this is not a correct method; perhaps, as suggested for the "yellow gene" mice, the agriculturist should learn to test each animal for the level of each of the catalysts suspected in limiting growth and other productive rates, such as the hormones of the pituitary, thyroids, adrenals, gonads, such groups

[1] The dairy cows in the United States, Great Britain, Canada, and New Zealand produce, on the average, 4,500 pounds of milk a year. The dairy cattle in Denmark produce, on the average, about 7,500 pounds. The Dairy-Herd Improvement Association cattle (in the U.S.A.) currently produce from 8,000 to 10,000 pounds a year.

[2] The average production in Missouri in 1945 was 152 eggs. The farm demonstration flocks averaged 178 eggs, and the high individual record was 354 eggs under R.O.P. supervision. Thirty years ago the average Missouri hen laid about 80 eggs per year; 20 years ago the average was about 100 eggs. The greatest increase in average production has been in the past five or six years.

as sulfhydryl enzymes, and such tests as basal metabolism and configuration of electromagnetic fields (Burr), just as the nutritionist analyzes foods or feeds for their vitamins, amino acids, and minerals in relation to their limiting effect on growth rate and other productive processes. Here is a capital problem worthy of the efforts of the best academic as well as agricultural investigators.

There is indeed evidence that rates of growth, milk production, and egg production may often be accelerated, for example, by administration of thyroid hormone or thyroactive protein. On the other hand, reducing the thyroxine level by feeding goitrogenic substances, such as thiouracil, decreased the growth rate but increased the fattening rate. A female sex hormone was observed to effect growth and fattening rates, as does thiouracil (L. W. Taylor), although by a different physiological mechanism. Male sex hormone, on the other hand, tends to increase growth rate rather than to increase fattening rate. These results point to the definite possibility that the hormonal balance is a major factor in the control of productive and reproductive rates.

The body chemistry, especially its catalytic components, will undoubtedly receive ever greater attention in its bearing on rates of agriculturally productive processes and also on neoplastic growth.

The outstanding needs in agriculture are yardsticks for measuring productive levels and methods for predicting productive potentialities in young animals. Just as methods have been developed for early recognition of intellectually gifted children, so methods must be developed for *early* recognition of productive capacities in farm animals. Rapidity of growth and fattening may well be correlated with the levels of some catalysts, nutrients, metabolic rate, electrical configuration, and so on. These levels may perhaps in turn be used to predict future performance in the young without resorting to the laborious progeny testing.

The Rate of Aging

Next to growth rate, the aging rate is the most important factor in the over-all economy of animal production. Dairy cattle, for example, do not pay for themselves in milk and calves until they are about four years old, and the longer thereafter they maintain a satisfactory yield in milk and calves, the greater the clear profit on the growth investment. The same holds true for poultry, for work stock (horses and mules), and for all breeding stock, especially those that are progeny tested.

Unfortunately, the rate of growth, and therefore the rate of maturing, is correlated with the rate of aging: the earlier an animal matures, the earlier it grows old and the earlier it dies. This correlation could be predicted from C. S. Minot's classic generalization of 1889, that "retardation of growth is old age." It was also demonstrated by the caloric underfeeding experiments of Osborne and Mendel (1914–15) and especially by those of McCay and Maynard (1941). About 1940 R. Schoenheimer, employing isotopes of hydrogen and nitrogen as tracers, observed that there is continuous renewal of body nitrogen. But as this metabolic interchange occurs at an ever-decreasing rate with increasing age, the *proportion* of young tissue declines with increasing age. This decrease in young tissue or increase in old tissue constitutes the basic aging process reflected by progressive dehydration, reduction in chemical reactivity and elasticity, and quantitatively measurable in man by the decline in accommodation range of the eye. The latter is most rapid at the earliest ages on which data are available. This harmonizes with Minot's theory of aging and also with the theory that body tissues are colloids and, like other colloids, age with time.

The problem of retarding the aging rate—the search for the fountain of youth—is, of course, as old as human thought. It has already been noted that delay in aging of rats was accomplished by caloric underfeeding. Mention may be made of similar earlier experiments by Waters, Trowbridge, Moulton, Haigh, and associates on steers at the University of Missouri (1919), by Childs on planarian (1915), and the recent ones on rats by Carlson and Holtzel (1946). Overeating on calories, particularly if derived from fat, is known to reduce life expectancy.

With regard to hormonal methods of control of aging, it has also been noted that thyroxine or thyroprotein appears to "rejuvenate" old fowls as measured by egg production and rams as measured by fertility.

We have defined aging as decrease in metabolic exchange, decrease in the replacement rate of old "building stones" for new ones. Would thyroxine, for example, which apparently accelerates such a metabolic exchange, delay or accelerate the aging rate—that is, provided it was administered at certain optimal levels? Similar questions might be asked about other hormones. It is not original to suggest that sex and other hormones may have "rejuvenating" effects when administered at certain levels, but it is new to investigate this idea seriously and to apply the results to increase agricultural production.

The Effects of Environmental Temperature

The internal physicochemical environment of the body, including its hormone and enzyme levels and nutrients, is dependent not alone on its heredity and nutrient supply but also on the physical environment, including temperature, light, humidity, air movement, barometric pressure, and so on. This is shown, for example, by the 30-per cent decrease in blood calcium level in fowls when the environmental temperature is increased from 70° to 90° F. (Conrad, 1939), a common temperature fluctuation, and by decrease in egg-shell thickness and egg size (D. C. Warren, 1940). The rate of milk production and the level of solids in the milk, especially fat and protein, decline steadily with rising temperature above 70° F. The growth rate in all domestic animals declines with rising temperature above 70° F., and, of course, muscular activity tends to decline rapidly with increasing temperature.

One basic thermal fact relating productivity with environmental temperature is that even unproductive living involves a large energy expense. Most of this energy is dissipated in the form of heat. The production of milk, eggs, body tissue (growth), and muscular work is associated with the production of huge quantities of heat, partly because there is a work, and therefore a heat, component in these activities, but mostly because of the heat increment of feeding, the so-called specific dynamic effect, which is the heat production associated with the intermediate chemical reactions in the body, the transformation, for example, of hay into body tissue or milk, and the heat production associated with the excretion of the waste products of such reactions.

A second basic fact is that environmental temperature affects profoundly the endocrine activities of the adrenals, gonads, and especially the thyroids. E. W. Dempsey and E. B. Astwood reported in 1943 that at 1° C. 100-gram rats produced 9.5 μg. thyroxine per day; at 25° C., 5.2 μg.; and at 35° C., 1.7 μg. C. W. Turner recently observed that fowls secreted 12 μg. thyroxine (in terms of d-l thyroxine) in cold midwinter but only 8 μg. in hot midsummer, and that there was a parallelism between thyroxine and egg production. The seasonal sex activities of most animals are associated with the day-to-night ratio (light), but temperature *per se* is also an important influencing factor. Most animals and plants are photoperiodic, but many are thermoperiodic. Photoperiodism and thermoperiodism may or may not be associated.

The long-range effect of high temperature is to reduce the body size (since the smaller the body, the greater the surface per unit weight and heat dissipated by way of the surface); to modify the body build so as to give the largest surface area; to develop sweat glands, since sweat vaporization is the most effective method for cooling the body; to reduce the amount and quality of fur; to reduce the amount of insulating subcutaneous fat; to develop protective coloration against light and therefore, in part, against heat; and especially to reduce heat production by reducing the level of muscular activity and of food intake. The apparent poise of the southern gentleman and the laziness of the "white trash" as well as of the dark are not products of race but of homeostatic mechanisms for protection against over-heating. The best way to keep cool in hot weather is to take it easy and eat sparingly, which are very unfavorable factors for high production. As has been mentioned, high temperature leads to depression of the activity of the thyroid and other endocrines. These combinations of circumstances lead to depression of the productive levels in hot and humid climates. The seasonal rhythms in fur production, subcutaneous fat deposition, sex activity, migratory activities, and muscular and other activities are dramatic illustrations of adaptation to environmental temperature and light. The mechanisms whereby these effects are accomplished are under investigation but not to the extent that they deserve to be.

Most of the careful investigations on the effects of the temperature complex on the reactions of organisms have been made on simple biochemical systems *in vitro* and on small poikilotherms which can be handled inexpensively. The sheer size of large farm animals places serious obstacles in the path of their investigation, so that but little scientific information is available on the effects of the temperature complex on farm livestock.

This is, evidently, a very important agricultural problem. Our best dairy cattle, for instance, evolved in equably cool maritime climates, such as Holland, Denmark, Scotland, and the Channel Islands, and their sweating mechanism—the chief cooling device in hot weather—is undeveloped. Yet they are concentrated in the Middle West and other regions subject to very high summer temperatures. The same holds true for virtually all our farm livestock. Selection of farm animals for high productive levels is not very helpful if unfavorable temperatures inhibit the realization of desirable potentialities.

The heat production is dissipated mostly by radiation at lower environmental temperatures, but as the environmental temperature rises, the function of heat dissipation by radiation, convection, and conduction is gradually taken over by moisture vaporization. Unfortunately, most farm animals do not sweat appreciably, and so the body temperature tends to rise when the environmental temperature reaches about 70° F. The animal then protects itself simply by reducing its activities. The decrease in the production of milk, eggs, body tissue, etc. with rising temperature is, then, in the nature of a homeothermic or homeostatic mechanism. It is not wholesome for nonsweating animals, or even for sweating man, to produce more heat in hot weather than is absolutely necessary, and they generally do not.

One thinks of two methods for increasing resistance to high temperature. One is biological, by crossing, for example, nonsweating cattle originating in cool Europe with the sweating cattle originating in hot Asia; the other is engineering, involving the control of the "private climate" of the animals. Both methods need investigation.

The Need for "Normal Standards"

We have seen that many factors influence the growth rate or production rate of farm animals, plants, and certain of their products. In order to investigate quantitatively the influence of each of these factors, it is necessary to have typical or average values, so-called "normal standards," for growth and aging.

There are generally accepted yardsticks for over-all growth, especially for growth in weight, but there are none for aging. Fortunately, the agriculturist is not interested in the over-all aging process, but rather in the aging of special functions, such as milk, egg, and wool production, fertility, and muscular-work ability. With the exception of work ability, the above criteria of aging are measurable, and the problem of muscular-work ability (in horses, mules, and asses) is at present under active investigation.

"Standards" for growth in weight, milk production, and egg production are available, but they are not without serious ambiguities. For instance, present-day white rats are larger and approach mature size at a different rate than those of 25 years ago because of selection and differences in methods of feeding and housing. The same holds true for other categories of animals. In brief, the standards, reference bases, and measuring rods themselves change with time and circumstance. Nonetheless, they are valuable for furnishing orienting backgrounds.

Standards are also needed for relative (allometric or heterogonic) growth—the relation of part to part and part to whole. For instance, the commercial value of a pig is not proportional to its gross weight alone but also to its dressing percentage and to the *relative* amounts of bacon, ham, loin, visceral organs, and so on. The value of a dairy cow is similarly dependent, not on its size but on the *relation* of its milk yield to size (maintenance cost). The value of a horse or mule is not dependent on its size alone but on the work it can do in relation to its size (maintenance cost); and so on with other productive processes. "Normal standards" are needed for these relations, and also an understanding of their significance.

Incidentally, one difference between a highly developed modern pig and an undeveloped one is in the bodily proportions at different ages and in the associated differences in their path of approach to the market size. J. Hammond and C. P. McMeekan (1928–40) demonstrated differences in the economy of pork and mutton production by controlling the speed of growth at different ages. This is a promising field of research on all categories of livestock.

Standards of age changes in growth efficiency (ratio of energy stored in the body to dietary energy, or feed required per 100 pounds live weight gain), and the influencing factors, are related problems of importance.

Normal standards are particularly useful if codified or generalized by rational equations—so-called "laws" of growth—having meaningful constants, constants which express quantitatively and meaningfully the productive rate and level at any given age and also represent the productive change with age.[3]

The relation between monetary profit and biologic efficiency also needs investigation. Profit depends not only on biologic efficiency of the process but also on many economic factors, such as costs of the labor, feed, housing, taxes, and other overhead expenses. For instance, two 800-pound cows producing as much milk and at the same energetic or biologic efficiency as one 1,600-pound cow are not as profitable, because the labor cost of milking, feeding, cleaning, housing, etc. is nearly twice as great for the former as for the latter. Goat, dairy cow, rat, mouse, and man produce milk at approximately the same biologic efficiency, but at quite different monetary cost.

In connection with the need for growth standards one thinks of the needs for sharply defined *biologic units,* especially units of mass and time. For instance, the basal energy and endogenous nitrogen metabolism per unit weight of a 0.05-pound (24-gram) mouse is about 20 times as great as that of a 1,200-pound cow. (The same relation probably holds true for feed consumption and milk production per unit weight.) The *biological* significance of a *physical* unit of weight is then about 20 times as great in a mouse as in a cow. Likewise, the rate of approach to mature body size is about 20 times as great in a 0.05-pound mouse as in a 1,200-pound cow. (The growth rate, *k,* in equa-

[3] The following equations are simple and useful for representing the three categories of growth mentioned: $Y = Ae^{kt}$ (1); $Y = A - Be^{-kt}$ (2); $Y = aX^b$ (3). Equation (1) represents the self-accelerating phase of growth prior to the major inflection of puberty in animals or flowering in plants; it may also be used for representing the rate of aging. Equation (2) represents the self-inhibiting phase of growth following the major inflection. Y is size of the animal, plant, or function at age t; k is the relative growth rate (or percentage rate when multiplied by 100) with respect to growth already made, Y, in equation (1), and with respect to growth yet to be made to reach mature size, A, in equation (2). The constant, k, in equation (2) is, then, the numerical value of the speed of approach to mature size, A; e is the base of natural logarithms. Equation (3) represents the relation of part, Y, to whole, X, and the exponent, b, is the relative increase in Y when the increase in X is 1.0. For instance, when the value of b is 0.5, it means that the part, Y, grows 50 per cent as rapidly as the whole, X.

tion (2)[3] is 0.8 for mice and 0.04 for cows.) This means that the *physiological* significance of a *physical* unit of time is about 20 times as great in the mouse as in the cow. *Physical* mass and time thus have different *physiological* significance in different species, individuals, and ages. Physical units of time are therefore ambiguous when applied to biological processes. There is need for clarification of *physiologic* units of mass and time. In the same category is the need for determining physiological equivalence of time and mass in different species of animals, so as to enable the transfer of experimental results from one species, individual, or age, to other species, individuals, or ages.

SUMMARY

It appears that while the immediate objectives of the agriculturist differ from those of the academic biologist, the long-range needs for standards of growth and aging, for physiologically equivalent units of time and mass, and for knowledge of the influence and mechanisms of various internal and external factors on growth and related processes are the same for both. This suggests that these two groups of biologists should work together more closely.

Technical Papers

Cardiac Failure in Cattle on Vitamin E-free Rations as Revealed by Electrocardiograms[1]

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During the past 8 or 10 years, in connection with an extensive study designed to determine the role of vitamin E in the nutrition and reproduction of cattle, a considerable number of the animals fed vitamin E-free rations throughout their entire lives have died suddenly and without evident cause as revealed by gross post-mortem examinations. The deaths have occurred among animals of both sexes and at ages ranging from 18 months to 5 years. The manner and suddenness of the deaths strongly suggested that the heart was involved. A variety of effects of vitamin E deficiency have been reported in different species of animals, muscular dystrophy in some form being the most common. Recently Houchin and Smith (*3*) produced muscular dystrophy in vitamin E-deficient New Zealand white rabbits 5 weeks of age. They found such animals to be highly susceptible to the action of the posterior pituitary extract, being killed by much smaller doses than were easily tolerated by controls receiving α-tocopherol. The dystrophic rabbits were, however, more resistant to normally lethal doses of cardiac glucosides. Radiographic examinations of the thorax showed the probable existence of cardiac dilatation. They concluded that the sudden death which occurs in advanced cases of muscular dystrophy is due directly to cardiac failure.

The electrocardiograph is constantly being used in the study of heart conditions in human subjects. That it can be put to similar use with the bovine has recently been shown in the comprehensive studies of Alfredson and Sykes (*1, 2, 4*) and Sykes and Moore (*5*). With these facts as a basis, beginning on 2 November 1945 and at monthly intervals or oftener thereafter, electrocardiographs were obtained on all animals on experiment. The instrument used and methods employed were essentially the same as those of Alfredson and Sykes (*1*).

Selected recordings indicating the progressive changes that occurred in the cardiac cycle of E541 are presented in Fig. 1. This heifer is the only animal that has died since the electrocardiogram recordings were started. Her dam and sire were both raised on vitamin E-free rations and died suddenly in the same manner as their daughter. E541 was born on 8 July 1944, was bred on 19 February 1945, and calved normally on 27 November 1945, when less than 17 months old. She died suddenly on 4 April 1946.

Study of the series of electrocardiograms obtained on this animal reveals that a gradual and progressive change occurred, the later recordings showing definite indications of the presence of cardiac abnormalities. The first definite changes appear in the recordings of 21 December 1945, as shown by an increase in P–R interval, a condition which persisted throughout the remaining records. The QRS complexes in Leads II and III also were changed, the

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